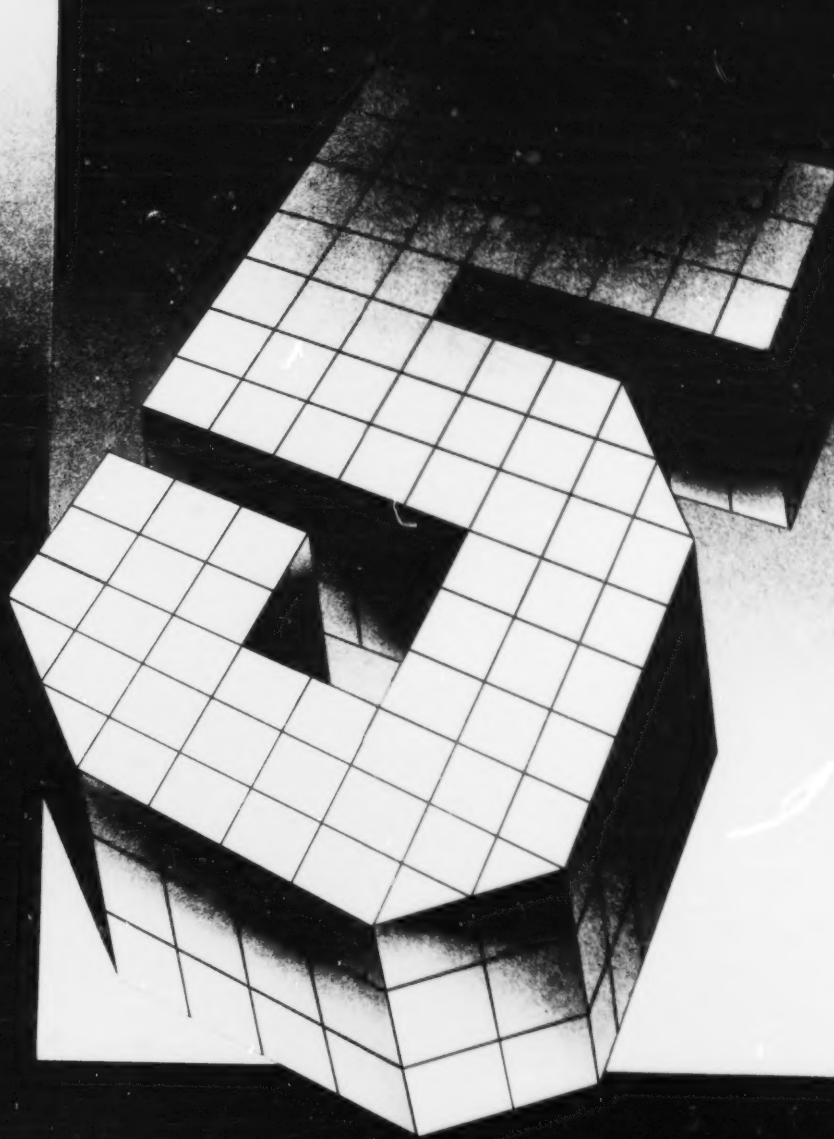


**ALBERTA HERITAGE FOUNDATION
FOR MEDICAL RESEARCH
5TH ANNUAL REPORT 1984-85**



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NEW DIMENSIONS

There comes a point in the life of every organization when people begin asking: Well, what have you accomplished? What do you have to show?

Asked that question after five years, The Alberta Heritage Foundation for Medical Research would line up thousands of people.

Here are Alberta's diabetics. Their physicians have a new source of counsel in the researchers who sort out the cause of diabetes and sift through the welter of new therapies.

Here are the heart attack patients who look to the U of C cardiac research unit where physicians and basic scientists pursue the cause of sudden cardiac death, develop new methods for diagnosis and treatment, and test new drugs.

Here are patients hospitalized for viral infections. They are cared for by Foundation-supported specialists who divide their time between hospital and research lab. Here are the victims of Alzheimer's disease, multiple sclerosis, epilepsy, and other neurological disorders. So far there are few, if any, therapies for these mysterious "black box" diseases but more scientists have been recruited to tackle neurological problems. Alberta patients have new opportunities to be diagnosed earlier and to participate in clinical research.

Here are Alberta's emerging medical graduates, rigorously trained by researchers to question all aspects of medical practice and to carefully evaluate the results of clinical research.

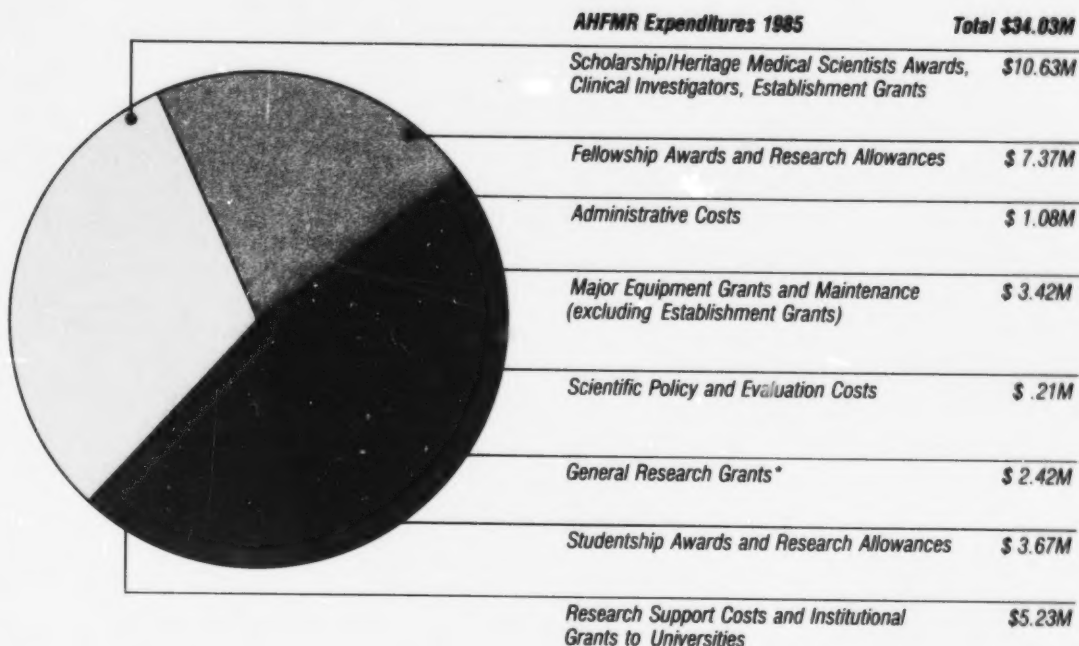
Here is the long line of the researchers themselves, 87 senior scientists recruited from Alberta, the rest of Canada and abroad. After five years the original Heritage Scholars hold up awards of distinction, multiple published papers, and some very concrete fruits of their studies. For example, one Scholar has developed a new method for making less expensive and more potent antibiotics. Another Scholar has developed an innovative technology for diagnosing osteoporosis and monitoring treatment in ways never possible before.

Behind the researchers are the graduates they train and at least 200 eager students each year. Some of these students are privileged to work in specific areas never before available in Alberta universities, for example, interdisciplinary studies in nutrition.

Other people touched by the work of the Foundation are less visible. Hundreds of scientists, physicians, nurses, dentists, and psychologists attend Foundation-sponsored national and international conferences bringing the best people here to focus on important health care questions. Then there are the laboratories which have state-of-the-art equipment funded by the Foundation to keep researchers on the competitive edge. Often the researcher who advances most quickly is the one with superior technological back-up.

After five years, the Albertans can confidently claim Foundation support has fostered a well-developed research community by building on existing strengths and adding entirely new thrusts. Members of this community contribute to improved patient care directly through service where they apply laboratory advances to patient problems, and indirectly through teaching others. Most important, the scope and depth of AHFMR supported medical research promises new hope for managing and preventing disease.

AN OVERVIEW



*Conference Grants, Visiting Scientist Grants, Travel Grants to Universities, Independent Establishment Grant and Research Professor-in-Residence.

In November 1979 an Act of Legislature created the Alberta Heritage Foundation for Medical Research to establish and support a balanced, long-term program of medical research based in Alberta. Foundation activities are directed toward the discovery of new knowledge and the application of that new knowledge to improve health care of Albertans and all people.

To build a balanced program, the Foundation supports basic and clinical scientists, both well-established people and young people beginning new research careers. Investigators explore a broad spectrum of disciplines such as: biochemistry, microbiology, pediatrics, immunology, neurology, dentistry, pharmacology and many others.

The Foundation is supported by a \$300 million endowment fund which generates interest revenue for operating expenses. The Foundation stands at arm's length from the government under the management of a group of distinguished Trustees.

Awards and Grants

The main activity of the Foundation is an awards and grants program designed to establish a critical mass of career scientists in Alberta. The program includes:

- Heritage Medical Scientist, Scholarship, and Clinical Investigatorship Awards
- Studentships (full-time, part-time, and summer)
- Fellowships
- Establishment Grants for New Investigators
- Grants for Major Equipment
- Grants for Equipment Maintenance
- Research Professors-in-Residence
- Visiting Scientists to Alberta
- Visiting Scientists from Alberta
- Visiting Lecturers
- Visiting Professors
- Travel Grants
- Grants for Conference Support

Much of the Foundation's work is carried out on the advice of a Scientific Advisory Council with 13 members who represent the national and international medical scientific communities. The international nature of the Council ensures quality peer review according to the highest standards and facilitates ongoing communication with researchers throughout the world.

The Council and its committees review and advise the Foundation on applications for loans, grants, research projects and professorships.

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LETTER FROM THE CHAIRMAN

On behalf of the Trustees of the Alberta Heritage Foundation for Medical Research I am pleased to present the Fifth Annual Report covering 1984-85 activities. The increased expenditures and the extended grant program indicate the Foundation has significantly expanded the Alberta scientific community in numbers and quality to provide Albertans with improved health care.

Expenditures for the year ending March 31, 1985 amounted to \$32.7 million, an increase of \$5.1 million or 18.5% over the previous year. During the first five years the Foundation cumulatively spent \$100 million on scientific affairs. According to long range planning for the next five years, the Foundation expects such expenditures to total \$300 million. This total includes the \$60 million designated for two medical research buildings now in the planning stages for The Universities of Alberta and Calgary. Apart from this building commitment, the cumulative expenditures for the next five years represent a major increase in the funding of medical research based in Alberta.

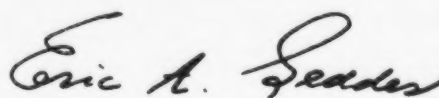
This level of spending will significantly affect the capital available in the endowment fund. As of March 31, 1985, the original \$300 million provided by the Legislature of Alberta had increased to \$436 million with the added unexpended investment earnings which remain available to the Foundation on a current basis. Because of the increased expenditures projected for the next five years, the endowment fund will likely be reduced to \$340 million by the fiscal year 1990-91, the tenth year of the Foundation's existence.

However, the Trustees agree that the endowment fund will require supplementation before that time. The Foundation has met with the Special Committee of the Heritage Savings Trust Fund to request the Legislature authorize supplementary funds before the end of this decade. After meeting with the Committee and after many formal and informal discussions with members of the Legislature, we believe they appreciate the work of the Foundation and the impressive results achieved by the universities within a relatively short period of time. In light of this, we are confident that our request for a supplement to the endowment will be supported with the full appreciation of our fundamental mission to Albertans.

During 1984-85 the Trustees approved a new program designed to assist the commercialization of university-based research. The initial response from entrepreneurial scientists has been enthusiastic and we believe the program will effectively stimulate the technology transfer process. The Trustees are convinced promoting the transfer of university-based technology to the commercial field will benefit academic medicine as well as the

economic well-being of the province. The Trustees will begin reviewing applications for the new program in November, 1985.

The Trustees again wish to record their deep appreciation of the leadership provided by our President, Dr. Lionel McLeod, who has guided the Foundation's activities with great devotion and skill during a period of considerable growth in our activities. In addition, we would wish to acknowledge publicly the contributions made by the devoted efforts of the staff of the Foundation.



Eric A. Geddes
Chairman

THE PRESIDENT'S REPORT

A major Foundation objective is to add substantially to Alberta's establishment of well-trained, motivated medical scientists. A target of 180 to 200 Foundation-funded research positions was adopted early as a guideline to the Foundation's financial planning. This number would not only permit strengthening of areas of existing high quality research but also provide the personnel for a significant number of new multidisciplinary research thrusts.

At the end of the fifth year, the Foundation is well on its way to the achievement of this objective. Eighty-eight new medical scientists have been recruited to our province in cooperation with Alberta's universities and their closely affiliated teaching hospitals and institutions. Thirty-eight have been established in Edmonton and fifty in Calgary. Alberta's medical scientists are supervising and guiding the training of some 160 graduate students and 150 post-doctoral fellows; clear evidence of a substantial investment in the medical research of tomorrow. These training programs provide bright young people firsthand research experience and place them on the road to a medical research career.

During the Foundation's fifth year, two special programs designed to encourage clinically qualified physicians into medical research training demonstrated their value; the Clinical Fellowship and the Clinical Investigatorship programs. Twenty-one clinical specialists undertook research training in first-class programs both in Alberta and in major centres in the United States, the United Kingdom, and France. Four well trained clinicians undertook to further their research experience as clinical investigators in plastic surgery, endocrinology and reproductive medicine, immunology and oncology, and in virology. The success of the first years of these programs suggest strongly that they will strengthen both research undertaken by physicians and strengthen the bridge linking basic and clinical research.

The influx of new medical scientists into groups or clusters has been most satisfying. This arrangement of research ensures effective communication, promotes collaborative research and improves efficiency in the use of high cost technical resources.

Another major achievement is the substantial increase in the impact of our Province's medical research upon patient care programs. Several examples are highlighted clearly within the body of this report.

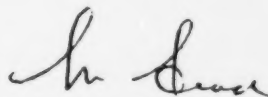
The new Heritage Medical Research Buildings, funded by Institutional Grants to The University of Alberta and The University of Calgary, will prove important in furthering multidisciplinary research thrusts. During the past year, the universities have begun planning and design work and construction should commence in the forthcoming year. These

buildings will provide the environment essential to multidisciplinary and collaborative work bringing together scientists from a variety of disciplines to focus their efforts on important medical problems.

During the year, the Foundation carefully studied the needs of Alberta's medical scientists working to commercialize new ideas and concepts. These studies resulted in a new technology transfer program to support the preliminary and early research necessary to attract commercial investment. This program will be implemented in the forthcoming year.

In the course of the year, hundreds of applications for support under the Foundation's programs were received, evaluated, and recommendations provided to the Trustees of the Foundation. The Foundation is indebted and deeply grateful to the many medical scientists in Alberta and beyond who so willingly devoted time and thought to evaluate these many proposals. Peer and multidisciplinary review is essential to the ultimate quality and value of Alberta's medical research effort.

The Foundation is fortunate to have a small, highly efficient office staff whose conscientious efforts contribute greatly to the successful operation of the programs. The outstanding commitment and enthusiasm of the Trustees of the Alberta Heritage Foundation for Medical Research maintains the strength and integrity of the Foundation.



Dr. Lionel E. McLeod
President



Coca

NEW EDGES

Most medical research builds on past work emerging from a continuum of steadily accumulated knowledge. But from time to time novel technology or a focussed awareness of a specific health problem break open new directions in research. In 1984-85 the Foundation funded several areas of investigation new to Alberta universities. These areas represent growing edges in medical research. Here Heritage scientists may well prove to be pioneers not only in Alberta, but in the international community.

The Food We Eat

Can nutrition cure or prevent disease? The diet debate has attracted ardent converts and critics but there has been almost no Canadian medical research to answer the controversial questions.

Dr. Tom Clandinin, Heritage Scholar at The University of Alberta, is leading the search for answers. Originally a Ph.D. from Edmonton, he was recruited from The University of Toronto in 1984 to establish a multidisciplinary program integrating work in foods and nutrition, medicine, dentistry, pharmacy and agriculture.

One of Canada's few nutritional biochemists, Clandinin's basic research on cell membranes focuses on a wide range of human problems from the cradle to the rocking chair: What is the best infant formula? How does diet affect particular organs (liver, intestine, pancreas) and disease states? How does dietary fat affect aging of cells?

During 1984-85 the Foundation, in cooperation with The Universities of Alberta and Calgary, recruited scientists from: Australia, New Zealand, Sweden, Great Britain, The Netherlands, The United States, and Canada.

New U of C Sleep Lab

Snoring can be more than an irritating habit. It can be a symptom of a common, serious breathing disorder called obstructive sleep apnea. The condition is characterized by snoring, daytime sleepiness, heart problems and sometimes respiratory failure.

Heritage Medical Scientist Dr. John Remmers was the first to identify the disease while at The University of Texas and now continues his pioneering work at The University of Calgary. Remmers suspects sleep apnea may be particularly prevalent in the elderly, which may contribute to fatigue and even death from heart attack.

Remmers is exploring the exact nature of the airway obstruction that causes apnea and developing more effective therapies. He will also investigate what he believes is a related disorder, infant respiratory distress syndrome (crib death).

Remmers' U of C sleep lab is funded by the Foothills Hospital.

The Dangers of Sour Gas

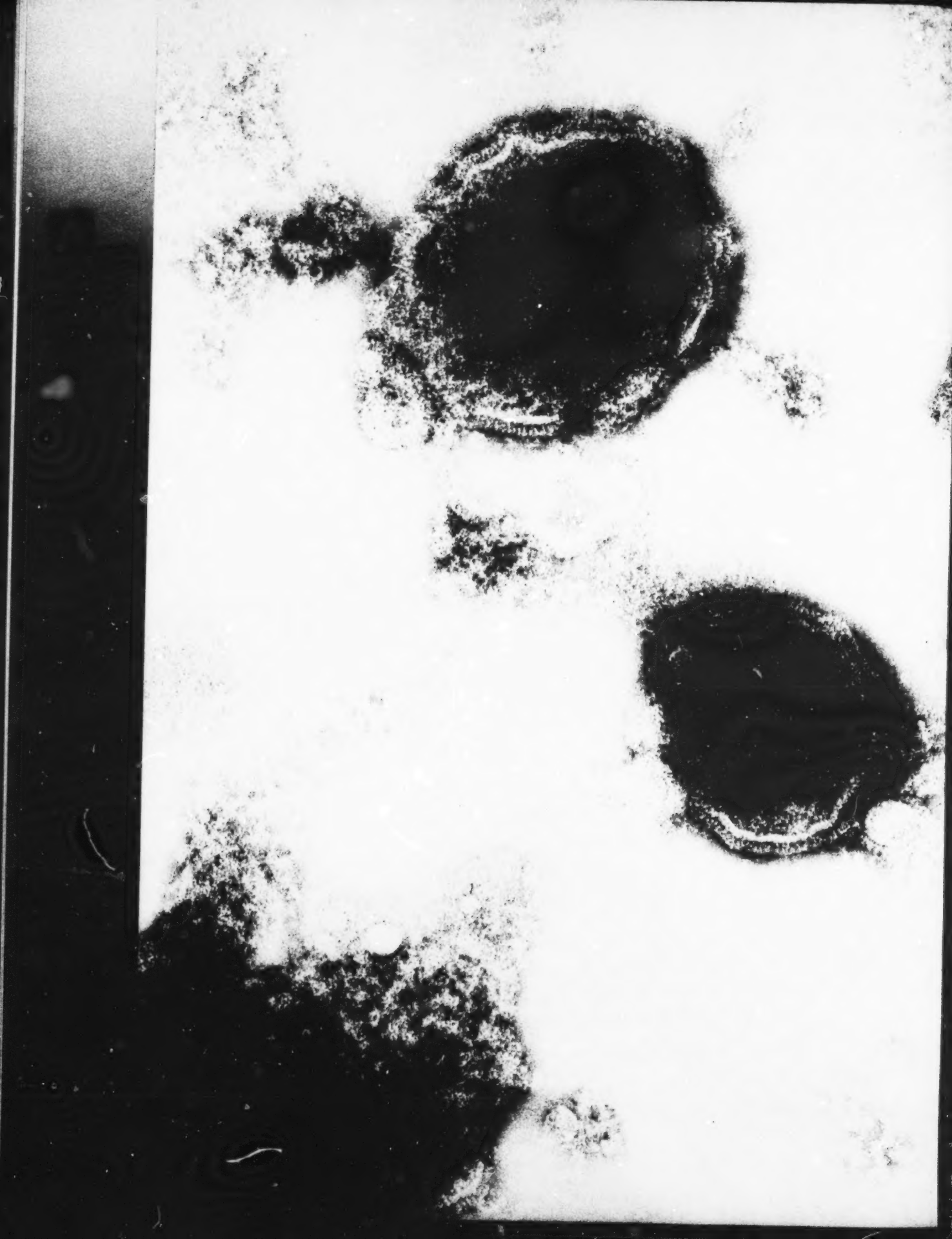
The oil and gas industry, so important to Alberta's prosperity, has its dark side. Oil field workers learn to work in the shadow of the threat of sour gas, never knowing when the deadly substance will suddenly appear or how it will affect them.

University of Alberta Heritage Scholar Dr. Bill Hulbert is studying the effects of sour gas on airway structure and function. This work provides the basis for further studies in effective treatment for injured workers.

"We simply don't know anything about it," Hulbert stresses. "We're at the point in H₂S research that we were 30 or 40 years ago with cigarette smoke."

Autism

Imprisoned in a private world, the autistic child cannot communicate even with those who love him or her. In the past, research attempts to understand the mysterious disorder have been frustrating because the autistic child is often retarded as well and the two factors are confused. Heritage Scholar, Catherine Lord has initiated one of the first long-term international studies of autism using a large sample of children with varying IQs. The research is conducted in collaboration with other scientists at The University of North Carolina and Maudesley Hospital in London, England. A clinical psychologist, Lord continues to practice at the Edmonton Glenrose Hospital.



ADDING STRENGTH TO STRENGTH

As is often the natural course of developments in the life of a university, Calgary and Alberta have developed definite areas of strength. Researchers in heart disease, growth and development, cell regulation, the neurosciences, and infectious diseases are gaining national and international recognition for their achievements.

Following logic and human nature, accomplished researchers attract more accomplished researchers who can be added to Alberta's scientific community because AHFMR funds are available to support them.

Heart Disease

Heart disease is still the largest single killer of people over 35 and half the fatalities result from sudden cardiac death. Cardiac researchers at the U of C are making significant headway in the battle against heart attack. They have developed techniques for identifying high risk patients with abnormal heart rhythms that often lead to heart attacks. They are devising new methods of treatment, particularly drugs and they have developed new ways of testing the effectiveness of drugs currently used.

Led by Heritage Medical Researcher, Dr. John Tyberg and Head of the Department of Medicine, Dr. Eldon Smith, the team covers the full spectrum of research from basic studies into the electrophysiology of the single cell to full-scale studies with heart disease patients.

In 1984 the Foundation funded two more people on the cardiac team. Electrophysiologist Dr. George Wyse, a member of the cardiac team previously funded by the Alberta Heart Foundation became a Heritage Scholar. Heritage Medical Scientist Dr. Henk ter Keurs was recruited from the Netherlands where he gained international recognition for his molecular studies of cardiac muscle.

Reproductive Medicine

In 1984 AHFMR successfully attracted one of the world leaders in reproductive medicine, Dr. John Maloney. He is former Director of the Monash University Centre for Early Human Development in Melbourne, Australia, the centre which pioneered much of the work on *in vitro* fertilization.

Fetal physiologist, Maloney is head of the U of C Reproductive Medicine Research Group, a natural outgrowth of the high risk pregnancy unit, and the three-year-old Infertility Clinic. Investigations cover the main concerns of reproductive medicine: care of pregnant women, their fetuses and newborns, birth control, infertility, and sexual dysfunction. This research thrust also adds strength to the well-established U of C Growth and Development Research Group consisting of 22 basic scientists.

Viruses

Viruses are proving to be more insidious and more deadly than ever suspected. The much-publicized viral link to AIDS is only one exciting finding in the exploding research field called virology. Recently viruses have been implicated in many disease states including multiple sclerosis, rheumatoid arthritis, juvenile diabetes, and some cancers.

In 1984 new Heritage Medical Scientist Dr. Aimo Salmi came from Finland to establish a research group on neurovirology at the U of A. He is an acknowledged world authority on the measles virus which occasionally develops into a persistent infection years after the childhood disease first occurs. This infection attacks the brain cells and eventually kills the victim.

In basic and clinical studies Salmi uses the measles virus as a model to understand persistent viral infections surfacing long after initial invasion. He also investigates multiple sclerosis, a disease he suspects may involve contact with a virus that compromises the natural immune system possibly years prior to the onset of the disease itself.

Salmi's expertise gives impetus and direction to the quality research already being conducted in infectious diseases by a number of scholars at both universities.

Calgary Scholar Dr. Robert Anderson is another new researcher in virology. He investigates persistent viral infection using a mouse model of hepatitis and the carrier mosquito for yellow fever.

Another new Heritage Medical Scientist, Dr. Ji-Won Yoon, was recruited from the National Institutes of Health in the United States for his pioneer work on the viral connection in juvenile diabetes. Yoon is the first scientist to discover concrete evidence of viral infection in children who have died from diabetes and he has developed a vaccine against viruses proven to cause diabetes in mice. His studies are part of the new Julia McFarlane Diabetes Research Unit at the U of C.

Heritage Scholar Dr. David Lau is another addition to the McFarlane team. An endocrinologist, Lau is investigating the biochemistry of obesity. With Dr. Daniel Roncari he has founded the new Outpatient Weight Control Clinic in The Foothills Hospital. The first of its kind in southern Alberta, the clinic offers a multidisciplinary approach to weight control, stressing modification of habits rather than diet.



PATIENT CARE

A Place to Turn

Alzheimer's Disease has become one of the feared diseases because as a dementing disorder it causes much heartache before the victim dies. A degenerating brain cell disorder with no known causes or cure, to some degree Alzheimer's affects an estimated 10,000 Albertans, primarily the aged.

Alzheimer's victims, their families, and physicians have a new source of help in The University of Calgary Dementia Clinic established by new Heritage Scholar Dr. Irma Parhad. The clinic provides critical diagnostic services to attempt to distinguish Alzheimer's from other treatable dementias such as those caused by infections or psychiatric disorders. Patients and their physicians are guided in the choice of therapies and given an opportunity to participate in research on the nature and treatment of Alzheimer's.

The Dementia Clinic is one of several specialty clinics headed by Heritage physicians who bring their research expertise to Alberta Health Care Services.

Dr. David Matheson, Director of the Immunology Clinic at The Alberta Children's Hospital cared for 250 people last year, a third of them adults. When a child suffers repeated infections and medical complications his physician suspects a basic immunology problem and refers him to the clinic. Matheson tests the child to see if he is subject to repeated transient illnesses because his immune system is immature or if there is a chronic congenital problem that must be treated with drugs.

As a pediatrician, Matheson treats and counsels people who have to live with a difficult medical problem. As a researcher, he takes the samples used for the advanced diagnostic tests into the lab to investigate the causes of immune deficiencies. For example, he has found evidence some long-term drug programs for various medical conditions may "insult" the immune system and weaken its ability to fight infection.

Two other Calgary Heritage Scholars have become resource diagnosticians, serving not only Alberta physicians but physicians throughout Canada. Dr. David Hoar offers prenatal screening for early identification of genetic diseases based on knowledge of DNA sequences with specific gene markers. The clinical work complements Hoar's studies on the search for new markers associated with genetic diseases such as neurofibromatosis.

Samples from all over Canada, the U.S., Britain, Mexico and Japan are sent to Dr. Marvin Fritzler to be analyzed for antinuclear antibodies that identify a carrier of disease sometimes years before the disease manifests illness. Fritzler is best known for his work on systemic lupus erythematosus, a devastating form of arthritis that often goes undetected in early stages because its varied symptoms mimic many other diseases.

The Physician-Researcher

The Foundation's new clinical research program attracts physicians who divide their time between laboratory bench and hospital bed. These specialists provide Albertans with an increasingly high level of medical care.

At the U of C virologist Dr. John Gill searches for a vaccine against herpes. He also investigates the efficacy of antiviral agents upon viruses, particularly some of those viruses which have developed a resistance to drugs parallel to the well-known phenomenon, antibiotic resistance. In the Foothills Hospital, Gill treats and counsels herpes patients and advises other physicians about general viral infections.

At The University of Alberta, Dr. Edmund Ryan cares for women who become diabetic during pregnancy. Because gestational diabetes generally lasts only the duration of the pregnancy but can reappear as diabetes later in life, it gives Ryan an excellent research model to study the causes of the disease.

Clinical Investigator, Dr. Jim Beauchene offers University of Alberta hospital patients his skills as a plastic surgeon. Beauchene's research activities have very concrete application. He is developing an innovative procedure for surgical reconstruction of wounds by capitalizing on the natural elasticity and growth potential of patients' own skin. A technique called therapeutic tissue expansion stretches or expands the skin. Limited clinical experiments by others have been encouraging but the physiological basis is unknown. Beauchene uses animal research to see if the expanded skin is new healthy tissue or inferior stretched skin. If it is new tissue as he believes, the therapeutic applications are exciting. Unlike skin graft, tissue expansion avoids the tissue match problem and reduces scarring.

Dr. Grant MacLean moves between the Cross Cancer Institute and his lab at the U of A where he explores the use of monoclonal antibodies to diagnose cancer and to target drugs for chemotherapy. MacLean moved to Edmonton from his native New Zealand because Edmonton provided excellent funding, a supportive environment for clinical research and respected colleagues like Dr. Michael Longenecker. His work focuses mainly on small cell lung cancer and ovarian cancer but is relevant to many malignancies. MacLean and his collaborators have successfully used monoclonal antibodies to picture cancer metastases in liver.



CLIMBING THE PATH

An 18-year-old who aspires to be a medical researcher faces at least eight years of post-secondary education. Nor is excellence in formal studies any guarantee of success because he or she must learn by doing as well as studying theory. An undergraduate, Ph.D. student or post-graduate student must learn from quality researchers in a competitively-funded lab if he or she is to gain the know-how and credibility to someday receive grants for independent studies.

Few young people can climb the long career path without help and until the advent of the Foundation, support in Alberta was seriously limited. The Foundation's extensive training program is designed to develop a mass of well-trained Alberta scientists. After five years the program is bearing fruit.

Ten years ago Cy Frank was a U of C med school rookie with a chronic knee problem from a baseball injury. Today he is an orthopedic surgeon and Heritage Scholar heading a new connective tissue lab at the U of C. He is investigating ligament healing in basic projects, conducting a survey of the source of knee injury, and doing knee surgery at The Foothills Hospital.

Frank exemplifies the bright, promising young person who deserves support. After he completed his orthopedic residency and specialty fellowship examinations, he studied for three years in Dr. Wayne Akeson's prestigious laboratory at The University of California supported by a Heritage Fellowship. Prior to returning to Calgary as a Heritage Scholar, Frank took an extended fellowship in Toronto to learn arthroscopy, (surgery using a fibre-optic telescope inserted in the joint).

Other Heritage Fellows have moved on to become independent scientists. A Fellow and now a Scholar at the U of C, Pam Sokol continues her investigations of a microorganism that causes many serious infections including an incurable chronic lung infection in cystic fibrosis patients. After a Fellowship under the supervision of Dr. Lorne Tyrrell at the U of A., Dr. John Gill is a Clinical Investigator studying herpes and other viruses at the U of C.

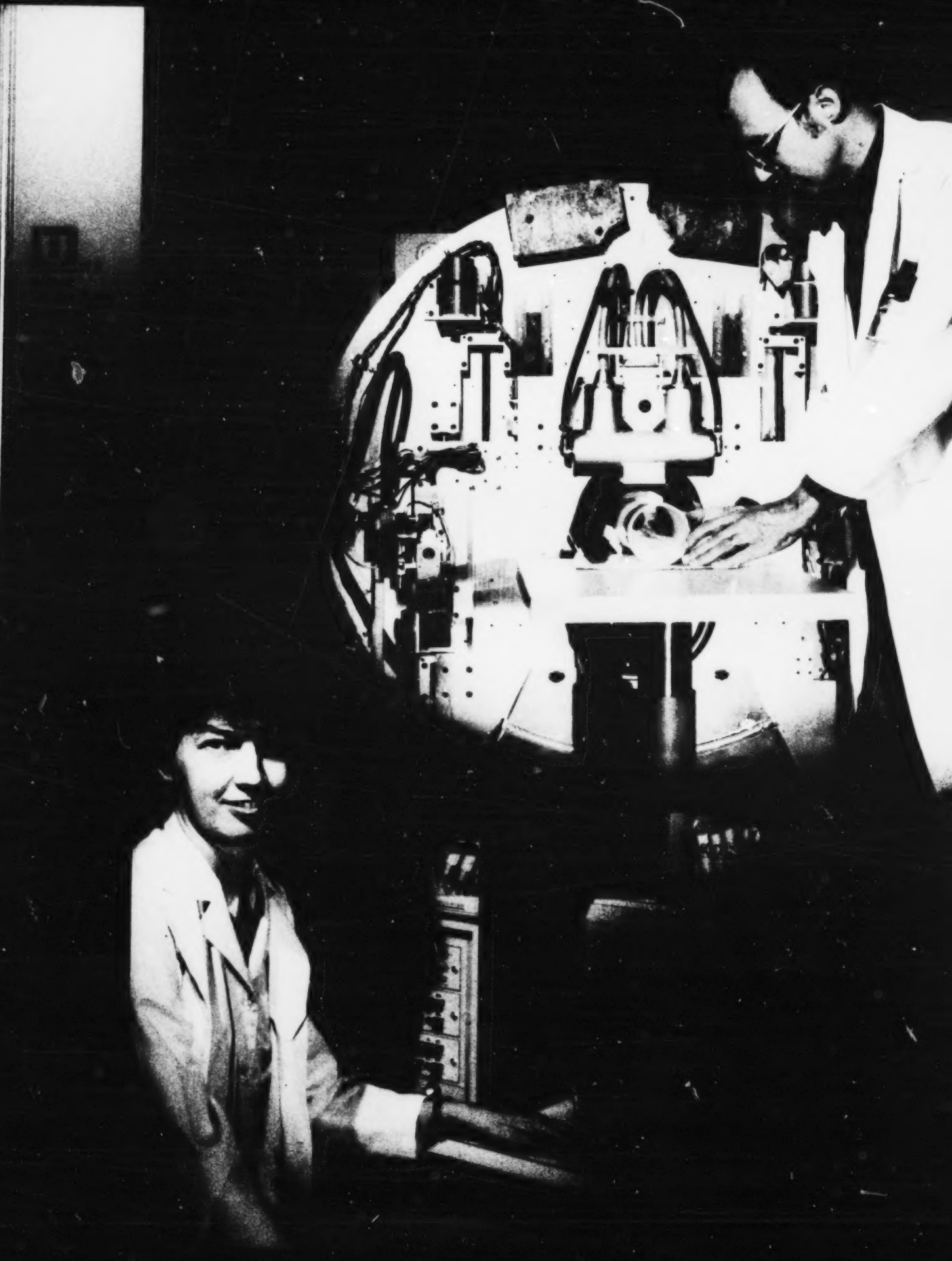
A number of Heritage Fellows are now taking advanced training under Clinical Fellowships in Alberta and abroad. For example, surgeon Dr. Norman Kneteman has a Clinical Fellowship to acquire beta cell transplantation techniques from Dr. Paul Lacy at Washington School University in St. Louis. Beta cell transplantation is one of the latest experimental therapies for diabetes. U of A Clinical Fellow Stephen Aaron is investigating why gold compounds found effective in treating arthritis cause toxicity in some patients, but not others. This extended training will help alleviate the critical shortage of clinical researchers who are so essential in the transfer of research findings to patient care.

The long road: On the average, Heritage Scholars with a Ph.D. have completed 11 years of post-secondary education. Clinical Investigators with a Ph.D. and M.D. have completed 15 years of post-secondary training.

Bright Young Lights

Students may be researchers-in-training but they are not simply assistants to established scientists. Many bright AHFMR students have contributed significantly to medical knowledge. For instance, Linda Ayer's Ph.D. studies focussed on the centromere antigen that reacts with antibodies in the sera of patients with scleroderma. Ayer studied under Dr. Marvin Fritzler at the U of C. Her knowledge of the antigen has important potential for understanding chromosomal abnormalities associated with conditions such as Down's syndrome and malignancy.

Another AHFMR student, Masao Fujinaga independently solved the three-dimensional structure of tonin, an important enzyme that has been implicated in the control of high blood pressure.



HIGH POINTS

Contrary to popular mythology, researchers seldom stumble upon serendipitous discoveries that send them running through the streets like Archimedes of bathtub fame. Usually the so-called discovery is a coming together of thousands of hours spent in the lab, most of them very routine. The high point culminates years of work by the researcher and by many colleagues as well.

Dr. Thomas Hangartner and Dr. Susan Jensen are examples of two scientists who experienced high points in 1984-85.

Dr. Hangartner, a physicist and computer expert was able to apply five years of engineering to patient care. Dr. Jensen, a microbiologist, cooperatively developed a new process for antibiotic production, work that has been taken up by other research labs and commercial firms.

Since its inception the Foundation has funded \$31 million of equipment in 257 laboratories. These funds provide state-of-the-art equipment such as electron microscopes that magnify particles one million times and computers that create three-dimensional illustrations of drug molecules.

New Antibiotics

U of A Heritage Scholar Susan Jensen and two colleagues have developed a new method for producing cheaper and potentially more effective antibiotics. Jensen, U of A microbiology chairman Dr. Donald Westlake, and Queen's University chemist Dr. Saul Wolfe employ an enzymatic cell-free system to short-cut the path to antibiotic production.

Jensen uses sound waves to break open the cell and extract the enzymes which trigger penicillin and cephalosporin antibiotics in fungi and bacteria. The enzymes are then applied to natural and synthetically modified substrates (starting materials) produced by Wolfe. Using this process, production is very rapid. Producing and refining more potent third generation antibiotics can take decades, but in Jensen's lab it may take as little as half an hour.

Because the new method cuts production time and therefore costs, it could lead to cheaper antibiotics for consumers. The process also provides opportunity for developing new antibiotics. The team has already produced a handful of promising ones.

The process is being patented and the team has been approached by pharmaceutical firms anxious to take the ground-breaking research to the next stages of drug development.

Early Osteoporosis Detectable

Sometime in their lifetime, usually after menopause, one in four women will suffer from osteoporosis, a disease in which bones lose their density and weaken. This frequently leads to broken hips, wrists, and spinal vertebrae fractures.

U of A Scholar Dr. Thomas Hangartner has developed a prototype CT scanner that allows physicians to diagnose osteoporosis early (the disease may build slowly for years), and to monitor treatment. A further development of x-ray technology, CT scanners use radiation to obtain data that is then translated into an image via computers. Hangartner's scanner precisely measures changes in bone density over time, something not possible with conventional CT scanners. Unlike other machines, Hangartner's distinguishes between compact bone and spongy trabecular bone which deteriorates first in osteoporosis.

Because the machine is so efficient, it requires one-twentieth of the radiation required by other scanners. This means it is safe to give patients multiple exposures and safe to evaluate healthy people in controlled studies on osteoporosis therapy.

In collaboration with Drs. Tom Overton and Charles Harley, Hangartner clinically tested the efficiency of Vitamin D to activate bone remodeling in postmenopausal women. The team found Vitamin D did have a positive effect and are now studying the influence of other potential activators.

The team is also being approached by a number of groups outside Alberta. The Medical Research Council has asked them to investigate how a corticosteroid called Prednisone affects bone. They are studying the influence of a diphosphonate on bone in multiple myeloma patients as part of a multi-centre trial for the National Cancer Institute. Proctor and Gamble also contracted the researchers to investigate phosphate and a diphosphonate on bone.

Perhaps the most satisfying endorsement of Hangartner's work came from the Alberta public. After the *Edmonton Journal* published a story on his research, Hangartner received 300 phone calls from women volunteering to participate in clinical studies.

CROSS TALK

Medical research is international and dynamic. Around the world scientists make advances faster than they can publish them and any researcher worth his electronic microscope is challenged to keep up.

AHFMR-sponsored conferences are an important way to keep Alberta researchers up to date and make their colleagues aware of developments coming out of Alberta. During 1984-85 the Foundation sponsored 19 workshops and conferences.

For example, an International Symposium on Insulin Dependent Diabetes Mellitus brought together leading scientists investigating everything from potential environmental causes of the disease to sensational experimental therapies such as cyclosporin treatment and beta cell transplants. The Symposium speakers included three prominent diabetes researchers at the U of C and the U of A: Dr. Ji-Won Yoon, Dr. Leigh Field and Dr. Martine Jaworski.

Another international symposium focussed on new directions in dental research and education to consider strategies for the expanding U of A program. A second dental conference brought together specialists who treat temporomandibular (jaw) joint problems.

One indication of productive medical researchers is success in national and international grant competitions from agencies such as the Medical Research Council of Canada. During 1984-85 Heritage Scholars received \$3.7 million in operating grants from competitive-funding agencies.

Controlling High Blood Pressure

If patients could see their family physicians' private offices they might spy a chart that outlined the definition and suggested treatment for high blood pressure. The chart is a direct result of a Foundation-sponsored conference on high blood pressure, a condition affecting one in every ten Canadians.

Nicknamed "the silent killer", hypertension is difficult to diagnose because it has no outward symptoms and people don't always have their blood pressure routinely checked. As well the level of pressure considered dangerous and requiring treatment is very controversial among physicians.

The Calgary conference brought together physicians and researchers to identify definitions of hypertension and make concrete recommendations for monitoring and treating the problem. The full report and ready-reference charts were published six months later in *The Canadian Family Physician*. This is one example where the best available knowledge on a major public health problem was accumulated and rapidly made accessible to family physicians.

Heritage Days

The annual Heritage Medical Research Days are an opportunity for Alberta researchers to exchange methodology on research results. Held November 15 and 16, the event this year featured 250 scientists who presented their work orally or in posters. Subjects ranged from new diagnostic techniques using a CT scanner to the effects of the drug Metronidazole on Crohn's Disease.

Four key speakers described their recent advances and shared the attitudes and methodologies they bring to the laboratory. Dr. Alan Bernstein of the Ontario Cancer Institute presented studies laying the groundwork for future gene therapy. Dr. Cyril Kay, Co-director of the MRC Protein Structure Group at the U of A discussed the role of calcium in muscle contraction. Dr. Robert Neer of Massachusetts General Hospital presented the results of clinical studies with parathyroid hormone on osteoporosis patients and Dr. Norman Shumway of Stanford outlined the story of heart-lung transplantation.

GRANTS AND AWARDS

Heritage Medical Scientist Award

This award was established to encourage the recruitment and establishment of senior medical scientists to Alberta. A Heritage Medical Scientist is a leader in his field and is internationally recognized for his scientific contributions.

Alberta investigators with a record of outstanding research, whose stipend from competitive funding agencies (MRC, NSERC, AHFMR, etc) is scheduled to terminate are also eligible.

Total number of awards: 5

Expenditures: (including establishment grants) \$2,731,858

Scholarships

Alberta Heritage Medical Research Scholarships support investigators recently trained in medical research who have demonstrated promise and ability to initiate and conduct independent research. A five-year, renewable Scholarship allows scientists to develop medical research unhampered by heavy teaching and service duties.

Scholarships are granted by competition and based upon the excellence of the candidate, the originality and importance of the project, and the quality and adequacy of the proposed research environment.

Total number of awards: 16

Expenditures: (including establishment grants) \$4,530,513

Clinical Investigatorships

Clinical Investigatorships give clinically qualified medical scientists holding full-time academic appointments further research training and experience assisted by competitively-funded basic or clinical researchers. Clinical investigators must have an M.D. or D.D.S., have completed clinical specialty training and two or three years of supervised medical research. The three-year award may be extended for two years but is not renewable.

Total number of awards: 4

Expenditures: \$774,983

Independent Establishment Grants For New Investigators

Heritage Medical Research Independent Establishment Grants are given to new investigators who are not funded by the Foundation (who may or may not hold an award from another research granting agency). This grant is designed to help new investigators quickly achieve maximal research productivity by providing equipment, technical assistance, materials and supplies.

Total number of awards: 20

Expenditures: \$1,392,723

Fellowships

Heritage Medical Research Fellowships provide qualified candidates with full-time post-graduate training in research in an area of medical science relevant to the aims of the Foundation. Fellows must have an M.D., D.D.S., D.V.M.,

Ph.D., or equivalent degree and must demonstrate high academic standing and evidence of research ability.

Awards are granted by competition based on excellence.

Total number of awards: Full-time (91)

Part-time (5)

Expenditures: Full-time \$2,656,420

Part-time \$ 49,338

Clinical Fellowships

Clinical Fellowships give individuals who have completed clinical training an opportunity to gain supervised medical research experience. The applicant must have a medical or dental degree obtained within the last ten years and have completed subspecialty clinical training. The one year award may be renewed three times.

Total number of awards: 21

Expenditures: \$945,376

Studentships

The Foundation provides three types of awards: Full-time, Part-time, and Summer Studentships.

There are a limited number of Full-Time Studentships for students registered in full-time M.Sc. or Ph.D. programs, and who plan careers in medical research.

The University must accept students into a graduate program and invite students to apply for an AHFMR Studentship. Studentships are granted by competition and awards are made on the basis of excellence.

A limited number of Part-Time Studentship awards are available to full-time students working towards professional health-related degrees, and seeking to spend substantial amounts of free time in medical research. Research required by the curriculum is not eligible for support.

Summer Studentship awards support promising Alberta university students who wish to spend their summer months (May to August) engaged in medical research:

Total number of awards: Full-Time 80

Part-Time 1

Summer 166

Expenditures: Full-Time \$1,157,600

Part-Time \$ 3,990

Summer \$ 633,707

Research Allowances

(Independently Funded Students & Fellows)

Holders of full-time Studentships and Fellowships awarded by another medical research agency using similar guidelines and standards are eligible to apply to the Foundation for a Research Allowance.

Total numbers of awards: Studentship 9

Fellowship 7

Expenditures: Studentship \$17,743

Fellowship \$27,000

Visiting Scientists

Awards for Visiting Scientists to Alberta enable a limited number of highly innovative and productive medical scientists to engage in medical research in an Alberta university for the purpose of bringing special knowledge and expertise to the host, the department, group, or institution.

Awards for Visiting Scientists from Alberta enable Alberta medical scientists to undertake collaborative research which they are unable to undertake locally due to inadequate technology or collegial expertise. Research funded must be an obvious step in the progression of a sustained research effort on the part of the Visiting Scientist.

The program allows Alberta's active researchers to participate in new and important break-throughs in medical research emerging elsewhere.

Total number of awards: 7
Expenditures: \$120,668

Visiting Professors

Heritage Medical Research Visiting Professorships are available for the purpose of recognizing and attracting truly outstanding medical scientists to visit Alberta to enrich and enhance the climate of medical research within the universities and the affiliated institutions active in medical research.

Total number of awards: 5
Expenditures: \$15,553

Alberta Heritage Medical Research Visiting Lecturers

The Visiting Lecturer program helps Alberta universities attract outstanding medical scientists who can broaden and enrich the educational experience of graduate students and fellows. The program also gives Alberta investigators, individually or in groups, the opportunity to discuss their research with other experts in their field of medical research.

Block Grant to Universities
Expenditures: \$362,300.00

Alberta Heritage Medical Research Travel Grants

The Foundation annually gives Travel Grants to The University of Alberta and The University of Calgary to be administered by the Universities for the following purposes:

Attendance of faculty members at workshops, conferences and annual meetings.

Recruitment of researchers.

Short visits to discuss complicated experimental design and cooperative research and prepare publications stemming from cooperative research.

Short visits to other laboratories to study new research procedures and techniques and to host external invest-

igators who can assist in the establishment of procedures and techniques.

Block Grants to Universities
Expenditures: \$245,700.00

Professors-in-Residence

The Foundation offers a very limited number of Heritage Medical Research Professors-in-Residence Awards to provide a special opportunity for Alberta faculty members to spend one year in full-time research free of teaching and administrative responsibilities. The award is intended for the investigator whose research has achieved a point at which concentrated effort might be expected to result in unusual levels of productivity and important new knowledge. The award is not a substitute or supplement to regular university leave opportunity.

Total number of awards: 1
Expenditures: \$33,500

Conference Grants

The Foundation supports a limited number of conferences and workshops clearly related to the enhancement of medical research in Alberta and the transmission of significant new knowledge to those responsible for the management of patients.

Conference support is usually limited to the funding of a small number of distinguished medical scientists invited to participate as special lecturers or major participants. Funds also support a limited number of workshops on collaborative research and workshops which explore and evaluate new research fundings.

Total number of awards: 19
Expenditures: \$298,749

Grants for Major Equipment

Major Equipment grants permit the University on behalf of investigators to purchase equipment essential to high-quality research. Applications usually relate directly to research projects supported by competitive granting agencies.

Grants for Equipment Maintenance ensure adequate maintenance of major equipment wholly funded by the Foundation's Major Equipment Grants. Preferential consideration is given to expensive facilities providing support to groups of researchers and multidisciplinary projects, especially those facilities offering services to researchers with partial or full recovery arrangements for regular operating costs.

Total number of Major Equipment and Maintenance Grants: 49
Expenditures: (includes installation and maintenance) \$2,408,575

REVIEW PANEL MEMBERS

Dr. Peter Allen, Professor, Department of Applied Science in Medicine, Faculty of Medicine, The University of Alberta.

Dr. Marvin Bala, Professor & Head, Department of Medicine, University Hospital, Saskatoon, Saskatchewan.

Dr. Mark Bisby, Professor, Department of Medical Physiology, Faculty of Medicine, The University of Calgary.

Dr. John Colter, Professor & Chairman, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. Joe Davison, Department of Medical Physiology, Faculty of Medicine, The University of Calgary.

Dr. Grant Gall, Professor, Department of Pediatrics, Faculty of Medicine, The University of Calgary.

Dr. Tessa Gordon, Associate Professor, Department of Pharmacology, Faculty of Medicine, The University of Alberta.

Dr. David Hart, Chairman, Immunological Sciences Research Group, Department of Microbiology & Infectious Diseases, Faculty of Medicine, The University of Calgary.

Dr. David Hoar, Associate Professor, Department of Medical Biochemistry and Pediatrics, Faculty of Medicine, The University of Calgary.

Dr. Ross Hodgetts, Professor, Department of Genetics, Faculty of Science, The University of Alberta.

Dr. Susan Jensen, Associate Professor, Department of Microbiology, Faculty of Medicine, The University of Alberta.

Dr. Yvonne Lefebvre, Associate Professor, Department of Medical Biochemistry, Faculty of Medicine, The University of Calgary.

Dr. Ernest McCoy, Professor, Department of Pediatrics, Faculty of Medicine, The University of Alberta.

Dr. Grant McFadden, Associate Professor, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. W. Paranchych, Professor, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. Keir Pearson, Professor, Department of Physiology, Faculty of Medicine, The University of Alberta.

Dr. Richard Peter, Professor & Chairman, Department of Zoology, Faculty of Science, The University of Alberta.

Dr. Jutta Preiksaitis, Assistant Professor, Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, The University of Alberta.

Dr. Fred Quandt, Assistant Professor, Departments of Medical Physiology & Anatomy, Faculty of Medicine, The University of Calgary.

Dr. Harvey R. Rabin, Professor, Department of Microbiology & Infectious Diseases, Faculty of Medicine, The University of Calgary.

Dr. R. Reithmeier, Associate Professor, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. D.A.K. Roncari, Julia McFarlane Professor of Diabetes Research, Faculty of Medicine, The University of Calgary.

Dr. Sheldon Roth, Professor, Department of Pharmacology & Therapeutics, Faculty of Medicine, The University of Calgary.

Dr. N. Schachar, Associate Professor, Department of Surgery (Orthopedics), Faculty of Medicine, The University of Calgary.

Dr. Gilbert Schultz, Professor, Assistant Dean of Research, Department of Medical Biochemistry, Faculty of Medicine, The University of Calgary.

Dr. Gerry Scott, Professor, Director, Surgical Medical Research Institute, Department of Surgery, The University of Alberta.

Dr. Paul Scott, Associate Professor, Department of Oral Biology, Faculty of Dentistry, The University of Alberta.

Dr. David Severson, Associate Professor, Department of Pharmacology, Faculty of Medicine, The University of Calgary.

Dr. Richard Stein, Professor, Department of Physiology, Faculty of Medicine, The University of Alberta.

Dr. Alan B. Thomson, Professor, Department of Medicine, Division of Gastroenterology, The University of Alberta.

Dr. John Tyberg, Professor, Department of Internal Medicine & Medical Physiology, Faculty of Medicine, The University of Calgary.

Dr. Leonard Wiebe, Professor, Radiopharmaceutical Chemistry, Associate Dean (Research), Faculty of Pharmacy, The University of Alberta.

Dr. George Wyse, Professor, Departments of Medicine & Pharmacology & Therapeutics, Faculty of Medicine, The University of Calgary.

TABLE 1

Grants & Awards Implemented from April 1, 1984 to March 31, 1985

Category	Number and Value of Grants and Awards*			
	U of A	U of C	Other	Totals
Studentship				
— Full-time	\$ 549,860 (38)	\$ 578,800 (40)	\$ 28,940 (2)	\$1,157,600 (80)
— Part-time	—	3,990 (1)	—	3,990 (1)
— Summer	400,493 (105)	225,214 (59)	8,000 (2)	633,707 (166)
Fellowship				
— Full-time	1,285,235 (45)	948,230 (33)	422,955 (13)	2,656,420 (91)
— Part-time	19,534 (2)	29,804 (3)	—	49,338 (5)
Independent Research Allow.				
— Studentship	6,804 (3)	10,939 (6)	—	17,743 (9)
— Fellowship	—	13,000 (3)	14,000 (4)	27,000 (7)
Scholarship/Est. Grants	1,936,240 (5)	2,594,273 (11)	—	4,530,513 (16)
Clinical Investigators	616,983 (3)	158,000 (1)	—	774,983 (4)
Clinical Fellowships	90,455 (2)	319,795 (7)	535,126 (12)	945,376 (21)
Heritage Med. Scientist/ Establishment Grants	284,788 (1)	2,447,070 (4)	—	2,731,858 (5)
Independent Est. Grants	781,788 (6)	610,935 (4)	—	1,392,723 (10)
Major Equipment Grants	1,041,692 (29)	1,345,383 (19)	—	2,387,075 (48)
Equipment Maint. Grants	21,500 (1)	—	—	21,500 (1)
Conference Grants	150,459 (9)	148,290 (10)	—	298,749 (19)
Professor-in-Residence	33,500 (1)	—	—	33,500 (1)
Visiting Scientist to Alberta	51,402 (2)	47,996 (3)	—	99,398 (5)
Visiting Scientist from Alberta	21,270 (2)	—	—	21,270 (2)
Visiting Professors	12,240 (4)	3,313 (1)	—	15,553 (5)
TOTALS	\$7,304,243 (258)	\$9,485,032 (205)	\$1,009,021 (33)	\$17,798,296 (496)

*Values shown are committed amounts on the effective date of award.

TABLE 2

Applications Received from April 1, 1984 to March 31, 1985

Category	Number of Applications Processed															
	U of A				U of C				Others				Totals			
	#Appl	A	R	W	#Appl	A	R	W	#Appl	A	R	W	#Appl	A	R	W
Studentship																
— Full-time	108	46	60	2	75	52	18	5	8	2	6	-	191	100	84	7
— Part-time	1	1	-	-	1	1	-	-	-	-	-	-	2	2	-	-
— Summer	186	132	50	4	109	82	26	1	9	3	5	1	304	217	81	6
Fellowship																
— Full-time	88	38	48	2	89	57	30	2	28	19	9	-	205	114	87	4
— Part-time	-	-	-	-	1	1	-	-	-	-	-	-	1	1	-	-
Independent Research Allow																
— Studentship	6	4	2	-	3	3	-	-	-	-	-	-	9	7	2	-
— Fellowship	2	-	2	-	3	3	-	-	-	-	-	-	5	3	2	-
Clinical Fellowship	11	3	8	-	10	7	2	1	10	7	3	-	31	17	13	1
Clinical Investigator	4	-	-	1	2	1	-	1	-	-	-	-	6	1	-	2
Clinical Traineeship	-	-	-	-	1	1	-	-	-	-	-	-	1	1	-	-
Scholarship/Est. Grants	16	7	9	-	15	9	5	-	2	1	-	-	33	17	14	-
Heritage Medical Scientist/ Establishment Grants	-	-	-	-	2	1	-	1	1	1	-	-	3	2	-	1
Independent Est. Grants	5	1	4	-	4	1	3	-	1	-	1	-	10	2	8	-
Major Equipment Grants	68	29	38	1	41	17	24	-	1	-	1	-	110	46	63	1
Equipment Maintenance Grants	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	-
Conference Grants	7	7	-	-	8	8	-	-	1	-	1	-	16	15	1	-
Visiting Professors	4	3	1	-	2	1	1	-	-	-	-	-	6	4	2	-
Visiting Scientist to Alta.	7	3	4	-	9	3	5	1	-	-	-	-	16	6	9	1
Visiting Scientist from Alta.	4	3	1	-	3	1	2	-	-	-	-	-	7	4	3	-
Special Initiative Funding																
— Major Equipment	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	-
— Research Support	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	-
TOTALS	520	280	227	10	378	249	116	12	61	33	26	1	959	562	369	23

A = Approved R = Rejection W = Withdrew

TABLE 3

Grants and Awards Renewed/Continued During the Period of April 1, 1984 to March 31, 1985

Category	Number of Grants and Awards Renewed/Continued			
	U of A	U of C	Other	Total
Studentship				
- Full-time	105	53	3	161
- Part-time	2	1	-	3
Fellowship				
- Full-time	74	50	23	147
- Part-time	1	5	1	7
Independent Research Allowance				
- Fellowship	1	2	7	10
- Studentship	5	5	3	13
Scholarship/Establishment Grants	22	35	-	57
Heritage Medical Scientists	1	4	-	5
TOTALS	211	155	37	403

TABLE 4

Total Number of Awards Implemented as of March 31, 1985, for the Following Award Categories

Category	U of A	U of C	Other	Total
Clinical Investigators	3	1	-	4
Scholarship/Establishment Grants	32	41	-	73
Heritage Medical Scientists	2	8	-	10
TOTALS	37	50	0	87

FINANCIAL STATEMENTS

Alberta Heritage Foundation For Medical Research

March 31, 1985

Auditor's Report

Balance Sheet

Statement of Revenue and Expenditure

Statement of Revenue Surplus

Notes to the Financial Statements

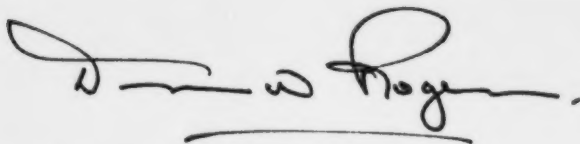
Schedule of Administration Expenses

AUDITOR'S REPORT

To the Trustees of the Alberta Heritage Foundation for Medical Research

I have examined the balance sheet of the Alberta Heritage Foundation for Medical Research as at March 31, 1985 and the statements of revenue and expenditure and revenue surplus for the year then ended. My examination was made in accordance with generally accepted auditing standards, and accordingly included such tests and other procedures as I considered necessary in the circumstances.

In my opinion, these financial statements present fairly the financial position of the Foundation as at March 31, 1985 and the results of its operations for the year then ended in accordance with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

A handwritten signature in dark ink, appearing to read "D. W. Rogers", with a horizontal line underneath the signature.

*Douglas W. Rogers, F.C.A.
Auditor General*

*Edmonton, Alberta
July 11, 1985*

BALANCE SHEET

as at March 31, 1985

	1985	1984
ASSETS		
Cash	\$ 5,084,677	\$ 6,027,558
Accounts receivable (Note 3)	113,089	71,102
Accrued interest receivable	4,950	4,058
Prepaid expenses	8,981	2,794
Mortgages receivable (Note 4)	588,396	567,288
Fixed assets, at cost less accumulated depreciation and amortization	350,153	209,224
	\$ 6,150,246	\$ 6,882,024
LIABILITIES AND SURPLUS		
Accounts payable	\$ 1,499,338	\$ 837,582
Revenue surplus	4,650,908	6,044,442
	\$ 6,150,246	\$ 6,882,024

The accompanying notes are part of these financial statements.

STATEMENT OF REVENUE AND EXPENDITURE

for the year ended March 31, 1985

	1985	1984
REVENUE		
Transfers from the Alberta Heritage Foundation for Medical Research Endowment Fund	\$32,000,000	\$31,000,000
Interest	640,534	630,060
	32,640,534	31,630,060
EXPENDITURE		
Scientific affairs:		
Scholarship and establishment grants	6,950,395	6,416,400
Fellowship grants and research allowances	6,660,212	6,143,662
Studentship grants and research allowances	3,670,918	3,083,212
Major equipment and maintenance grants	3,419,863	5,702,701
Heritage medical scientist grants	3,184,706	1,312,457
Research support costs	2,252,069	1,734,717
Institutional grants	2,176,863	1,070,077
Independent establishment grants	1,282,044	448,872
Building program grants	750,000	300,000
Clinical fellowship grants	713,911	—
Clinical investigatorship grants	490,756	—
Visiting lecturer grants to universities	340,375	336,475
Conference support grants	300,545	314,254
Travel grants to universities	205,953	254,916
Visiting scientist grants	146,802	271,577
Independent research allowances	105,973	108,567
Recruitment and planning grants to universities	28,735	30,052
Research professor-in-residence	26,056	8,000
Program development	25,358	—
Visiting professor honoraria and travel grants	16,463	26,663
	32,747,997	27,562,602
Administration expenses, Schedule 1	963,279	941,373
Scientific Advisory Council expenses	138,858	143,568
Trustee expenses	112,609	113,437
Other committee expenses	71,325	75,568
	34,034,068	28,836,548
Operating surplus (deficit) for the year	\$ (1,393,534)	\$ 2,793,512

STATEMENT OF REVENUE SURPLUS

for the year ended March 31, 1985

	1985	1984
Revenue surplus at beginning of year	\$ 6,044,442	\$ 3,250,930
Operating surplus (deficit) for the year	(1,393,534)	2,793,512
Revenue surplus at end of year	\$ 4,650,908	\$ 6,044,442

NOTES TO THE FINANCIAL STATEMENTS

March 31, 1985

Note 1 - Authority

The Alberta Heritage Foundation for Medical Research operates under the authority of the Alberta Heritage Foundation for Medical Research Act, Chapter A-26, Revised Statutes of Alberta 1980.

Note 2 - Significant Accounting Policies and Reporting Practices

Transfers from the Alberta Heritage Foundation for Medical Research Endowment Fund:

Section 8 of the Act provides that money required by the Foundation shall be paid from a \$300,000,000 Endowment Fund at the request of the Foundation. The Act also provides that payments shall not be made if they would result in the cost value of Endowment Fund assets being less than \$300,000,000. On this basis, the total available for transfer to the Foundation as at March 31, 1985 amounted to approximately \$136,000,000.

Depreciation and Amortization:

Furniture and equipment is depreciated on a straight line basis at the rate of 10% per annum to a maximum of 90% of cost. Leasehold improvements are amortized on a straight line basis over the term of the lease.

Changes in Financial Position:

A statement of changes in financial position is not provided as disclosure in these financial statements is considered to be adequate.

Note 3 - Accounts Receivable

Accounts receivable consist of the following:

	1985	1984
Unexpended grants held by universities:		
Travel	\$ 54,277	\$ 14,530
Visiting lecturer	41,496	19,572
Grant refunds	—	20,000
Miscellaneous	17,316	17,000
	<u>\$113,089</u>	<u>\$ 71,102</u>

Note 4 - Mortgages Receivable

Mortgages receivable represents the unpaid principal on mortgage advances to research scientists.

Note 5 - Commitments

As at March 31, 1985 the Foundation had committed the following amounts for scientific affairs expenditure:

Building program	\$58,950,000
Scholarship and establishment grants	11,316,664
Heritage medical scientist grants	7,025,017
Fellowship grants and research allowances	2,791,072
Major equipment and maintenance grants	2,535,289
Institutional grants	2,208,796
Studentship grants and research allowances	1,292,456
Clinical fellowships and investigatorships	840,252
Independent establishment grants	737,268
Special initiative grants and research allowances	285,400
Visiting scientist grants	117,116
Conference support grants	59,800
Professor-in-residence	7,445
Visiting professor honoraria and travel grants	5,942
	<u>\$88,172,517</u>

These commitments pertain to the following fiscal years:

1985-86	\$25,970,557
1986-87	23,749,545
1987-88	26,695,265
1988-89	11,437,939
1989-90	302,940
1990-91	16,271
	<u>\$88,172,517</u>

Note 6 - Approval of Financial Statements

These financial statements were reviewed by the Audit Committee and recommended for approval by the Trustees.

SCHEDULE 1

Schedule of Administration Expenses for the year ended March 31, 1985

	1985	1984
Salaries	\$ 484,656	\$ 424,090
Rental of premises	97,802	99,303
Depreciation and amortization	65,448	47,681
Employee benefits	63,399	51,775
Public relations and advertising	62,916	92,495
Stationery, printing and office supplies	52,498	64,510
Travelling and accommodation	35,968	25,118
Telephone	20,779	9,937
Vehicle	15,290	15,601
Maintenance	14,763	22,304
Consultant fees	14,421	56,254
Postage and courier	12,054	11,859
Staff training	8,014	—
Recruitment	4,334	5,992
Purchased services	3,102	3,218
Accounting and legal fees	3,025	5,854
Insurance	2,817	4,762
Miscellaneous	1,993	620
	\$ 963,279	\$ 941,373

APPENDIX

Alberta Heritage Foundation for Medical Research

Appendix of Awards

Heritage Medical Scientists

Scholarship Awards

Clinical Investigators

HERITAGE MEDICAL SCIENTISTS

ALLEN, Peter, Ph.D.

Professor

Department of Applied Sciences in Medicine
Faculty of Medicine, The University of Alberta

Date of Appointment: 83/01/01

IMAGING AND BIOCHEMICAL APPLICATIONS OF NMR TO MEDICINE

Nuclear magnetic resonance (NMR) imaging is a new non-invasive technique for obtaining a picture of a cross section of part of the body. Though the technology has been used in physics and chemistry for several decades, it has only recently been applied to medicine with the advent of sophisticated computing technology.

The medical applications of NMR are most exciting and promising because the technique is safer and more productive than conventional imaging methods. Unlike the x-ray CT scanner or the PET scanner, NMR imaging does not use potentially harmful x-rays or unstable nuclei. Instead, it works on the principle that when certain stable atomic nuclei are placed in a magnetic field and stimulated by radio waves of a particular frequency, they will re-emit some of the absorbed energy in the form of radio signals. This is called NMR. The strength and frequency of the radio signals are then fed into a computer which translates the information in an accurate image with high resolution or contrasts.

NMR is particularly suited to medical imaging because the nucleus of the hydrogen atom in water gives rise to the largest NMR signal from all stable nuclei and water is the major constituent of the human body. Since many disease states are characterized by an alteration in fluid levels, NMR could be a powerful diagnostic tool. It also means NMR effectively images soft tissues complementing x-ray technology which detects rigid body structures more easily.

NMR technology can also be applied to yield information about the function of body tissue (compared to x-rays which only yield information about structure). In NMR spectroscopy scientists have a probe to observe chemicals deep within the body so that bodily processes can be studied in a normal state, in a diseased state, and under the influence of medical treatment. In the future, scientists expect NMR spectroscopy will enable them to observe tumor growth, or monitor how nerve cells deteriorate in nerve degenerating diseases, and then observe how such conditions respond to therapy.

In 1984 Allen and his team members refined the customized small animal machine and tested a variety of complex procedures to be sure the system delivers accurate information for specialized projects, particularly in localized spectroscopy.

Animal studies on stroke and tumor models were initiated and the procedures for structural imaging were established.

They also began experiments using NMR spectra from forearm muscle to see if fasting affects the function of muscle. This work is designed to establish a base line of information so that physicians in intensive care can accurately assess whether or not lung muscles have become strong enough for independent breathing so that the patient can be taken off the respirator. Presently the decision is based on increased body weight but this increase could be due to water rather than increased muscle bulk.

DAVISON, Joseph, Ph.D.

Professor

Department of Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/29

NERVOUS CONTROL OF GASTROINTESTINAL SECRETIONS

Control of the secretions of gastrointestinal glands is achieved by a complex interaction of nervous, hormonal and paracrine (local chemical) transmitters. Until recently, nervous control of glands was believed to be mediated by just two transmitters, acetylcholine (ACh) and noradrenalin and only three gastrointestinal hormones were positively identified. Scientists now know the digestive system manufactures, stores, and releases a large number of biologically active substances which might function as neurotransmitters, hormones or paracrine agents. Interest has focussed on a particular group of substances called peptides which are found in both the gastrointestinal tract and the central nervous system. The discovery of VIP, CCK/P, substance P somatostatin, and other so-called "brain neuro-peptides" establishes a new link between the gut and the central nervous system and blurs earlier distinctions once considered definitive.

Davison is investigating how pancreatic, salivary and gastric secretions are regulated by these peptides and other substances. He studies how established transmitters operate at the cellular level. For example, electrophysiological and biochemical methods enable Davison to study how nerve transmitters and other secretory stimuli affect membrane and intracellular events in glands. He also investigates the physiology of putative or supposed transmitters which may involve identifying and characterizing new peptides.

In other projects, Davison explores how the spontaneous movement and secretion or absorption in the gastrointestinal system is controlled by certain reflexes, particularly vagovagal and peripheral sympathetic reflexes.

Because the physiology and biochemistry of a gastrointestinal system is so fundamental to good health, this basic research will eventually lead to more understanding of many disease states.

In 1984 Davison and his colleagues conducted a number of studies on the nervous control of intestinal secretion which showed, among other things, that endogenous neural transmitters cause a secretion of chloride with little or no effects on the absorptive processes. They identified several of the transmitters involved. They also identified the structure and function of a number of the vagal pathways.

Another project demonstrated that cholecystokinin can function as an endogenous satiety agent to regulate food intake, depending upon the integrity of the vagus nerve.

These basic studies have progressed to the point where methods and concepts can now be applied to collaborative clinical studies of inflammatory bowel disease.

MALONEY, John, Ph.D.*

Professor

Departments of Obstetrics & Gynecology & Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/06/01

THE PHYSIOLOGY AND DEVELOPMENT OF THE FETUS AND NEONATE

The Reproductive Medicine Research Group was formed on June 1, 1984 to study the development of the unborn and newborn infant with the goal of reducing perinatal mortality and ill health. The first of a series of programs is a basic and clinical investigation into the perinatal period with particular emphasis on the physiology of the respiratory and cardiovascular systems during the last trimester, parturition and the immediate newborn period.

The 14 member group is unique in that it combines basic and clinical research using non-invasive techniques for fetal monitoring. For example growth and development of the human fetus will be monitored with ultrasound. This information will be combined with other data obtained more directly from animal experiments.

Maloney's research concentrates on three distinct areas: the physiology of labor, birth and the immediate neonatal period; the functional development of the respiratory system and cardiac function *in utero* and in the neonatal period; and the factors responsible for the structural growth and maturation of the respiratory system and heart in the perinatal period.

For example, one study examines the influence of tissue stress on lung development before birth, the preparation of the respiratory system for birth and its function in the immediate neonatal period. One pioneer experiment examines the development of neural activity in the vagus nerve as it affects the control of fetal and newborn breathing. The group is also studying hypoxia at birth, estimated to cause 80 percent of perinatal deaths. They are examining how hypoxia in late gestation affects the performance of the heart, and the biochemistry and ultrastructure of the myocardium.

The fundamental programs will lead into research on other problems that, like hypoxia, cause fetal and newborn death or mental and physical disabilities. These problems include: growth retardation, Sudden Infant Death Syndrome, premature labor and pulmonary immaturity.

McGHEE, James, Ph.D.

Professor

Department of Medical Biochemistry

Faculty of Medicine, The University of Calgary

Date of Appointment: 83/07/01

GENE EXPRESSION DURING ANIMAL DEVELOPMENT

The life of almost all animals begins with the union of sperm and egg to form a single cell, which then divides to produce the myriad of different cell types present in the adult organism. What are the important molecular steps in this process? How can one individual cell divide into two daughter cells that are biochemi-

cally different from each other? What kind of clock tells a cell when it is the right time to produce a product such as hair or teeth or blood? These are the fundamental riddles of developmental biology that McGhee is trying to approach.

All the above questions can be most conveniently studied in the small non-parasitic nematode, *C. elegans* and McGhee is using this worm as a simple model for the development of higher organisms, including humans. Because these worms are transparent, all cell divisions can be followed inside the developing embryo, obviously an impossible feat in the study of human embryos. In contrast to humans where there are upwards of a trillion cells with incredibly complex lineages, an adult *C. elegans* has less than a thousand cells and the cell lineages are known exactly. Moreover, worms can be quickly grown in huge quantities, the genetics are superb and genes cloned and altered by modern recombinant DNA methods can be injected back into the adult gonads to see how they behave during embryonic development.

As a convenient molecular marker of development, McGhee is studying the appearance of several digestive enzymes in the embryonic intestine. He has identified one particular enzyme, an esterase, that appears very early in the developing gut. The cell lineage indicates that there are only three cell divisions at which the decision to express this esterase can have been made. McGhee is using a combination of microscopy, biochemistry, genetics, and recombinant DNA technology to discover the chemical instructions that tell these digestive enzymes to turn on at the correct time, only in the gut and not, for example, in the muscles or nerves.

In 1984 McGhee further developed his experimental model. He identified within one cell division when esterase activity occurs and found esterase expression is independent of cell division and of complex three-dimensional cues from embryonic morphology. He has also purified the esterase protein to homogeneity and has mutated and mapped the esterase gene.

REMMERS, John, M.D.*

Professor

Department of Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/09/01

CONTROL OF BREATHING BY THE NERVOUS SYSTEM IN HEALTH AND DISEASE

Breathing is a vital, continuous action whose initiation and control emanates entirely from the brain. The neural activity responsible for this rhythmic motor act originates in the lower regions of the brain, in the medulla and pons. The neurons in this region generate respiratory impulses and are extensively interconnected forming a network that gives rise to the neural rhythm and controls its distribution to respiratory muscles. Remmers' overall goal is to understand how various members of this network influence each other to generate and control breathing. He also seeks to understand what alterations occur in disease that cause breathing to cease with potentially dire consequences.

The research projects focus on how one respiratory neuron influences the activity of another. In other words, Remmers asks: How does one member of the network talk to another? Com-

munication among respiratory neurons is accomplished through the release of chemical substances called neurotransmitters. An electrical signal in one cell causes the release of a neurotransmitter which, in turn, either excites or suppresses electrical impulses in another. Such interactions among respiratory neurons underlie the generation of the respiratory rhythm and coordination of respiratory neural activity. However almost nothing is known about the nature of the identity of the respiratory transmitters or the nature of the interactions.

To fill these basic gaps in our knowledge, two requisite methods have been recently developed in Remmers' lab. One allows the stable, long term measurements of the electrical voltage in single respiratory cells of the brain of cats. The other allows local application of neurotransmitters and their blockers onto the surface of this cell while measuring its voltage. The results of these experiments will allow him and his colleagues to identify the neurotransmitters responsible for specific behavior of particular respiratory neurons at various times in the respiratory cycle.

The major disease resulting from a malfunction of the respiratory neuronal network occurs during sleep and is characterized by a total cessation of breathing, called apnea. This occurs in 1-2% of the population. Apnea results either from a failure of the respiratory neurons to generate a breathing rhythm or from a blockade of the air passage in the throat, so that despite vigorous breathing efforts, no breathing occurs. The goal of this aspect of the research is to elucidate the underlying cause of the failure of rhythm or airflow obstruction. This entails neuro-respiratory studies during sleep in which the activities of various respiratory muscles are recorded and the level of carbon dioxide and oxygen are monitored.

A related objective is to develop and perfect methods of treating sleep apnea. For obstructive sleep apnea, Remmers and his colleagues will develop new methods of applying positive pressure to the nose, thereby inflating the air passage in the throat and preventing its collapse. Using the knowledge gained in the study of respiratory neurotransmitters, drug therapy for obstructive sleep apnea and for failure of the respiratory rhythm will be developed.

Remmers has established a new Foothills Hospital Sleep Clinic to conduct clinical research on sleep apnea.

SALMI, Aimo, M.D., Ph.D.*

Professor

Department of Medical Microbiology

Faculty of Medicine, The University of Alberta

Date of Appointment: 84/08/01

IMMUNOPATHOGENESIS OF NEUROVIROLOGICAL DISEASES

Viruses usually cause acute infections but they may also lead to chronic diseases in animals and human beings as well. Viral infections of the central nervous system are of special interest because many of the so called slow virus infections causing long-term debilitating diseases are restricted to the brain. There are good reasons to believe that many chronic diseases of the central nervous system, including multiple sclerosis, are caused by slow viral infections. However, very little is known about virological and immunobiological mechanisms leading to such diseases.

Measles virus is one of the candidates for the etiology in many chronic diseases because of its ability to cause persistent infections both in cell cultures and in living organisms. However, very little is known about the mechanisms leading to persistent infection.

The main purpose of these studies is to reveal mechanisms of chronic virus infections by some RNA-viruses, especially measles virus. To understand the phenomena Salmi and his team of researchers are studying the virus structure, its immunology, and immunobiology as well as studying patient material. This basic research concentrates on a more detailed analysis of the surface proteins of the measles virus.

In a search for typical markers for measles virus chronicity, Salmi has recently produced a monoclonal antibody which seems to react with cells chronically infected with measles virus but not with cells from acute infections. He has further shown that this antibody binds to the RNA-polymerase of measles virus in chronically infected cells. Further research will investigate if such a change in measles virus polymerase could partially explain persistent infections by measles virus.

Since infection of lymphocytes could be one of the mechanisms of the immune deviations found in some chronic diseases, he has also initiated studies on virus-lymphocyte interaction using mumps and rubella viruses as well as the measles virus. Salmi hopes to find out which subpopulations of lymphoid cells are infected and if the nature of virus replication is different in different types of cells. He is also studying the effect of viral infections on the levels of soluble mediator molecules produced during immune response.

Because viral infections are more easily studied in animal models than humans, Salmi has initiated work on a rodent model. He has shown that mice can be used in immunological studies of measles virus antigens and begun work on animal models of demyelinating diseases such as multiple sclerosis.

Although he is originally concentrating more on basic studies, he has also completed a collaborative clinical study on patients with subacute sclerosing panencephalitis (SSPE) which is a chronic and often lethal form of measles virus infection. He demonstrated that immune complexes are very frequently found both in the serum and cerebrospinal fluid of such patients, that their level fluctuates, and that they are at least partially composed of the measles virus antigens. These observations help explain some of the immunopathological features in chronic measles virus infections. He also continues collaborative work with Finnish colleagues on the virology and immunology of multiple sclerosis.

TER KEURS, Henk, M.D., Ph.D.*

Professor

Department of Medicine and Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/10/01

ACTIVATION AND CONTRACTION OF THE HEART

Pump function of the human heart may be compromised by diseases such as coronary artery disease that limits the blood supply to the heart muscle, arrhythmias and intrinsic diseases of heart cells. Diagnosis and therapy of these conditions are limited

by gaps in our understanding of the mechanical properties of the cardiac cell and of how contraction is controlled by the process that couples the heart's electrical activity with contraction. Ter Keurs' goal is to elucidate the mechanisms of heart muscle contraction and understand the processes that modulate the mechanical performance of the muscle.

Activity of the heart is initiated by an electrical process that occurs at the membrane of the cardiac cells or the action potential. During the action potential calcium ions flow into the cell. This induces release of even more calcium from stores in the cell which leads to contraction. Calcium ions are subsequently taken up by the stores and pumped out of the cell so that the cells relax to their resting state. Ter Keurs particularly focuses on how heart rate and drugs affect the calcium balance of the cells. These studies will serve to refine a model of excitation contraction coupling. The model will then be used as a diagnostic tool for studies of heart disease patients.

A consequence of extrusion of calcium ions from the cell which occurs in exchange for sodium ions, is a depolarization of the membrane. Calcium overload of the cells may thus induce spontaneous action potentials and eventually arrhythmias in damaged myocardium. (Arrhythmias are irregular heart beats which accompany heart failure.) Ter Keurs will use an experimental model of this process to elucidate its mechanism and to study the effect of antiarrhythmic interventions including drugs and hormones.

The observation that the heart automatically adjusts its output to the inflow of blood from the body was described more than half a century ago. It has been explained on the basis of increased ability of the cardiac proteins to contract when the protein system is extended. Length dependent performance is not a unique property of the heart. It appears to manifest itself in all contractile cells and probably results from a basic property of contractile proteins. It also has been well established that contraction is started by binding of calcium ions to the contractile proteins actin and myosin. Ter Keurs' second major research effort investigates the effect of calcium ions on the dynamics of contraction to test the hypothesis that the affinity of the contractile proteins for calcium ions depends on the length of the cell.

TYBERG, John, M.D., Ph.D

Professor

Departments of Medicine and Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/07/01

CARDIAC MECHANICS: FACTORS AFFECTING THE HEART'S PUMPING ACTION

Tyberg is investigating cardiac mechanics, most particularly the effects of pressure exerted by the sac around the heart called the pericardium. Tyberg and his associates have challenged established dogma by demonstrating that, with one exception, the effect of the pericardium cannot be measured by a conventional open catheter as is common clinical practice.

Doctors have mistakenly assumed pericardial pressure equalled intrathoracic pressure, but Tyberg has shown the contrary. This has important implications for the treatment of heart failure patients.

Other studies explore heart-lung interactions by measuring surface pressure between the lung and the pericardium during volume loading and positive end expiratory pressure. Identifying how much pressure the lungs exert on the heart may prove to be very important in patients with emphysema, pulmonary edema and fibrosis.

Tyberg is also investigating how certain drugs which have empirically been proven valuable, actually work. Preliminary work with the drug angiotensin (which decreases venous volume with little change in pressure) and the drug nitroprusside (which lowers pressure while maintaining or increasing volume) indicates certain agents change pericardial pressure by changing the capacity of the veins.

A fourth area of research involves the mechanics of nonischemic myocardium (healthy area of muscle in the heart wall) adjacent to the ischemic area (area with deficiency of blood supply). Whether these areas perform normally or are actually depressed by an as-yet unknown mechanism is not clear.

Tyberg conducts both basic and clinical work in collaboration with eight other members of the Cardiovascular-Respiratory Research Group.

In 1984 Tyberg published his findings that pericardial pressure is virtually equal to right ventricular diastolic pressure in dogs and verified the results in collaborative clinical studies with Dr. Wilbert Keon of the Ottawa Heart Institute. The results of this work suggest pericardial pressure can be effectively estimated by measuring right atrial pressure.

Tyberg also acquired information on how nitroglycerin in the catheterization laboratory affects the pressure-volume relation in the left ventricle. Apparently LV transmural pressure can be predicted from the difference between pulmonary capillary wedge pressure and right atrial pressure and this clears the way for a number of important clinical investigations. Other work supported his hypothesis that vasoactive agents such as nitroglycerin and angiotensin shift LV diastolic pressure-volume relation by changing pericardial pressure.

WANG, Jerry, Ph.D.

Professor

Department of Medical Biochemistry
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/12/01

STUDIES IN CELL REGULATION

Living cells rely on an intracellular communication system to adjust cellular activities during changes in the external environment. The basic elements of this system are certain small molecules known as second messengers whose cellular concentration can be readily changed by disturbances from outside and whose function is to modulate various cellular processes. There are two general and universal second messengers: Ca^{2+} and cyclic AMP. The metabolisms and actions of these two messengers are interrelated by a host of enzymes and protein factors. The long term objective of this proposal is to elucidate the principles underlying the complex interactions in the communications system.

One of the major approaches is to select key enzymes and proteins for the study of their regulatory properties, and their inter-

actions with other components of the system. The present focus is on a Ca^{2+} -binding protein, calmodulin, which has been implicated in various cellular processes by regulating key enzymes or proteins in these processes. To elucidate the general mechanism of the action of calmodulin, the cyclic nucleotide phosphodiesterase is selected for detailed kinetic and thermodynamic study of its activation process. To investigate evolutionary and functional relationships among calmodulin-dependent proteins, as well as structure-function relationships of selected enzymes, monoclonal antibodies are developed as structure and function probes. Calmodulin-dependent protein kinases are studied to explore the complexity of the calmodulin regulatory system. A calmodulin-dependent phosphatase is studied in terms of its physiological significance. The protein kinases and phosphatase are selected for studies because they are expected to interact with many other proteins in the communication systems in the cell.

Another major approach is to use cultured cells to study calmodulin and calmodulin-dependent proteins under various culture conditions. These studies will illustrate how calmodulin functions in living cells and how calmodulin and its regulated protein may be controlled under different physiological conditions. The Cell Regulation Unit has obtained evidence to suggest calmodulin may function in controlling the phosphorylation states of tyrosine. The phosphorylation of protein tyrosyl residue has been implicated recently in the modulation of cell growth. Another finding is that cAMP phosphodiesterase, an enzyme which is involved in the metabolism of cAMP, a second messenger, exists as different isozymes in mammalian brain. This observation may lead to a better understanding of how the two major second messenger systems, Ca^{2+} and cAMP systems, are inter-linked.

In 1984 Wang and his team members produced two additional monoclonal antibodies which cross-react with different calmodulin dependent proteins, suggesting that calmodulin dependent proteins have a significant amount of homologous structure.

They also discovered three isozymes of a particular enzyme (bovine brain calmodulin-dependent cyclic nucleotide phosphodiesterase). Two have been isolated and found to have different regulatory properties. Wang acquired further evidence that under certain conditions a surge in intracellular calcium may activate various CAM-dependent processes without initiating cAMP degradation.

Other calmodulin studies initiated new research on the possible involvement of CaM in the regulation of cell transformation.

YOON, Ji-Won, Ph.D.*

Professor

Department of Microbiology & Infectious Disease
Faculty of Medicine, The University of Calgary

Date of Appointment: 84/10/08

TWO POSSIBLE MECHANISMS FOR THE PATHOGENESIS OF VIRUS-INDUCED DIABETES MELLITUS

It is known that insulin-dependent diabetes mellitus (IDDM) results from the destruction of pancreatic beta cells. Among several possibilities, acute viral infections and autoimmunity have been thought to cause the destruction of pancreatic beta cells in

genetically predisposed individuals. The hypothesis that viruses may be one cause of IDDM is supported by numerous case reports which have shown a temporal relationship between onset of certain viral infections and subsequent development of diabetes. The best evidence that viruses have a causative role in diabetes comes from experiments with animals. The development of encephalomyocarditis (EMC) virus-induced diabetes in mice is dependent on the genetic background of the host and the genetic makeup of the virus. The separation of the two stable variants, diabetogenic D variant (EMC-D) and the nondiabetogenic B variant (EMC-B), from the M-variant of EMC virus has made it possible to investigate genomic differences between these two pathologically distinct variants. Yoon's first objective is to isolate specific diabetogenic viral gene(s) from the EMC-D virus and to test its diabetogenic activity in genetically susceptible animals after the incorporation of the gene into the nondiabetogenic EMC-B viral genome. This information will elucidate the molecular basis of this form of IDDM.

Although a large percentage of IDDM may result from an autoimmune process directed against pancreatic beta cells, scientists do not know what triggers the autoimmune response. Hypothetical triggers range from genetical pre-programmed immunological abnormalities to environmental effects such as viruses and chemicals. Yoon's second objective is investigating how viruses can trigger autoimmunity leading to IDDM. He collects lymphocytes from patients with recent onset IDDM and examines them for viral antigens as well as virus particles. He also hybridizes cellular DNA (extracted from the lymphocytes) with cDNA probes for the human virus candidates. If this work proves fruitful, it could eventually lead to vaccines or antiviral chemotherapy.

Evidence regarding cell-mediated autoimmunity implicates autoreactive T-lymphocytes in the destruction of beta cells. This suggests that activated T-lymphocytes in early diabetics contain a subset of T cells which are beta cell antigen specific.

Yoon hopes to produce monoclonal antibodies against the autoreactive T cell receptors which have specificity for a beta cell specific antigen. Such a monoclonal antibody might prevent the autoimmune response.

In addition to cell-mediated autoimmunity, humoral immune responses have been found in the IDDM patients. The serum from many patients with IDDM have islet cell surface antibodies (ICSAs) which react with surface antigens on the plasma membrane of viable islet cells. Although the role of the ICSAs in the pathogenesis of IDDM is not clear, it has been reported that ICSAs inhibit the release of insulin from pancreatic beta cells and, in the presence of complement, ICSA-positive serum causes lysis of beta cells as measured by ^{51}Cr -release cytotoxicity assay.

Yoon aims to produce a monoclonal anti-idiotypic antibody against the cytotoxic beta cells surface antibody (CBSA) and test it for use in immunotherapy of IDDM patients. Through passive immunization, immunological therapy would suppress levels of CBSA and thus prevent pancreatic beta cell damage early in the course of the disease.

SCHOLARSHIPS

ANDERSON, Maurice, Ph.D.
Assistant Professor
Department of Pharmacology & Therapeutics
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/01/04

DEVELOPMENT OF NEUROMUSCULAR JUNCTION

This is a molecular study of the synaptic apparatus joining nerves and skeletal muscles. During embryonic development, growing nerves make contact with skeletal muscle cells and this generates specialized cellular structures at the forming motor end-plate. This poorly understood "trophic" or "inductive" interaction appears to also contribute to the maintenance of neuromuscular apparatus in adults. Degenerative diseases such as muscular dystrophy may involve lesions in these mechanisms.

Anderson uses monoclonal antibodies as probes to study the molecular structure of the neuromuscular junctions and also observes their formation in cell cultures.

In 1984 Anderson discovered evidence that proteolytic enzymes may be involved in signals between nerve and muscle cells.

ANDERSON, Robert, Ph.D.*
Associate Professor
Department of Microbiology & Infectious Diseases
Faculty of Medicine, University of Calgary

Date of Appointment: 84/09/04

CONTROL OF VIRUS SYNTHESIS ASSEMBLY

This is a study directed toward understanding how certain viral infections become persistent and result in slowly destructive diseases, often afflicting the nervous system. Using a mouse hepatitis model, Anderson examines the molecular events involved in replication in cell types which either do or do not support persistent infection. So far his work suggests persistence depends upon the host cell membrane because it apparently determines the extent to which infected cells become fused with neighboring cells.

In another approach to the question, Anderson investigates why yellow fever is a benign virus in the body of its carrier mosquito but very toxic in the human host.

BAZETT-JONES, David, Ph.D.*
Assistant Professor
Department of Anatomy
Faculty of Medicine, The University of Calgary

Date of Appointment: 84/09/17

ULTRASTRUCTURE OF TRANSCRIPTION COMPLEXES

This is a study of the mechanism whereby genes are expressed in the transcription of DNA to RNA. The transcription machinery of a particular cell does not read the whole library of genes but knows which are to be transcribed and where to start reading on any particular gene. If Bazett-Jones can discover how this occurs, it will lead to greater understanding of disease states where genes are deregulated such as in cancer.

To do this Bazett-Jones uses an innovative electron imaging spectrometer added to a transmission electron microscope. One

of three in the world, this equipment is revolutionary because it provides a picture of the structure and chemical make-up of biological particles, making it possible for the first time to map the element phosphorus which reveals how transcribed DNA strands are packaged.

BIDDLE, Fred, Ph.D.
Associate Professor
Department of Pediatrics and Medical Biochemistry
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

GENETIC STUDIES OF THRESHOLD TRAITS OF MAMMALIAN DEVELOPMENT

This is a study of birth defects which are genetically determined and are labelled "threshold traits" because not all individuals with a genetic disposition to express the defect do so. Cleft lip and spina bifida are examples of threshold traits. Using mouse embryos, Biddle is investigating the interaction between the genetic information, its control of developmental processes and variable environmental "insults" or factors.

He is also studying the cellular processes that regulate the normal segregation of the sex chromosomes (X and Y) in spermatocytes, again using the mouse model which includes a series of inherited mutations with birth defects. Since similar birth defects occur in man, these studies on genetic and environmental factors will increase our understanding of the probability of producing abnormal sperm.

In 1984 Biddle completed a nine-strain survey of mice with various malformations caused by chemicals called teratogens. He is currently doing a genetic analysis of the difference in reactivity.

BOISVERT, Donald, M.D., Ph.D.
Associate Research Professor
Department of Surgery
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

PATHOPHYSIOLOGY AND THERAPY OF CEREBROVASCULAR OCCLUSION

This is a study of brain damage following occlusion of a cerebral artery, commonly known as a stroke. While scientists know some irreparable brain damage occurs minutes after a stroke, recent investigations indicate variable amounts of brain tissue survive for hours or days in a "live" but non-functional state. The length of survival depends upon the severity and duration of the decrease in blood supply. Boisvert is identifying the factors which determine the level of residual blood flow during initial hours after the stroke occurs.

This study may lead to the development of emergency treatment strategies to minimize the destruction of brain cells in stroke patients.

In 1984 Boisvert initiated brain edema research using nuclear magnetic resonance to image the condition. He found a specific alteration in neurotransmitters plays a role in acute cerebral ischemia. He also investigated efficacy of a drug used to treat strokes.

BOURNE, Gregory, M.D.
Assistant Professor
Department of Physiology
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/10/28

THE REGULATION OF TESTICULAR GnRH RECEPTORS AND GnRH- LIKE PEPTIDES AND THEIR ROLES IN STEROIDOGENESIS

This is a study of interrelated hormones which regulate gonadal function, particularly a newly identified compound localized in the ovaries and testes. This new compound seems to function like GnRH, a peptide produced in the hypothalamus known to regulate production of eggs and ovulation in females and production of testosterone and sperm in males. The GnRH-like compound also appears to control sexual maturation and senescence.

Bourne's research may provide the molecular basis for the development of new drugs such as a male contraceptive, a treatment for precocious puberty, or a treatment for decreased gonadal function in old age.

In 1984 Bourne established an in vitro system which allowed him to determine the secretory profiles of two hormones related to the action of GnRH.

BOWLING, Douglas, Ph.D.
Assistant Professor
Department of Medical Physiology and Anatomy
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/14

PROJECTIONS OF SINGLE IDENTIFIED RETINAL AXONS

This study focuses on how the signals that come from the eye are interpreted by the brain. Bowling is investigating the role of a structure called the lateral geniculate nucleus (LGNd) located near the centre of the brain. Because this structure is the first place where signals from the eyes are brought together, determining its function will increase our understanding of how normal vision is affected by disease and injury. Bowling is testing evidence that indicates the LGNd is important for our ability to see fine detail and movement of objects.

Though this research is clearly relevant to fundamental questions regarding vision, it is also more generally applicable to other questions in neurological medicine.

In 1984 Bowling identified specific patterns in the receiving cells of the LGNd. These patterns reflect the specific patterns of axons that relay different kinds of information from the retina to the LGNd. Bowling identified the axonal patterns in his first years as a Heritage Scholar.

BULLOCH, Andrew, Ph.D.
Assistant Professor
Department of Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

CELLULAR BASIS OF ADULT NEURONAL PLASTICITY

This is a study of the capabilities of the adult nervous system to grow and adapt to change. This involves combined elec-

trophysiological and morphological study of adult molluscan neurons as they exhibit neurite outgrowth and synapse formation. Neurons are examined both within the normal environment of ganglia in organ culture and also as dissociated cell cultures. Additionally, neurite outgrowth can be invoked in situ by various manipulations involving trauma to the animal, but not directly damaging the nervous system. The goal of such studies is to determine the factors which can evoke growth and determine the specificity of synapses in the adult nervous system. This information is relevant to the treatment of injuries, paralysis and other disease states where nerves are damaged.

In 1984 Bulloch demonstrated adult molluscan neurons have differential ability to sprout into a central unknown environment. He also identified a new form of neuronal plasticity, again in adult molluscan neurons which exhibit sprouting when the animal is exposed to a variety of stresses.

BURKA, John, Ph.D.
Associate Professor
Department of Pharmacology
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/08/01

THE ROLE OF AA METABOLITES IN AIRWAYS HYPERREACTIVITY

This is a study of products of arachidonic acid (AA) which contribute to the tone of bronchial airway smooth muscle. In disease states such as asthma, there is increased synthesis and activity of broncho-constrictor agents. Burka is identifying the products of AA, determining their effect on airways physiology, and exploring mechanisms which could limit their activity. This study may lead to improved treatments for asthma.

Burka is also investigating two other diseases: gallbladder disease (role of AA metabolites) and rheumatoid arthritis (synovial fluid and leukocytes).

In 1984 Burka's research included a comparative analysis of how bronchodilator drugs affect airway contractions. He also began collaborative studies testing anti-arthritis drugs.

CARNE, Thomas, Ph.D.
Assistant Professor
Department of Chemistry
Faculty of Science, The University of Calgary

Date of Appointment: 81/09/01

BIOSYNTHESIS OF PITUITARY HORMONES

This is a study of enzymes in the pituitary gland which synthesize three peptides from a common precursor. These hormones control many aspects of the body's metabolism including synthesis of steroids, mobilization of lipid from the liver and adipose tissue, and salt and water reabsorption. Carne is identifying the products formed by reacting the enzymes with precursors synthesized from messenger RNA in vitro. He also works with synthetic peptides.

This research may lead to the development of new drugs which inhibit specific hormonal production and could be used to treat disorders such as Cushing's Syndrome where there is an excess of one pituitary hormone.

In 1984 Carne looked for the site where the precursor to active hormones are processed and found it is not located within secretory granules as other researchers suggested.

CLANDININ, Michael, Ph.D.*

Professor

Department of Food & Nutrition

Faculties of Home Economics and Medicine,

The University of Alberta

Date of Appointment: 84/07/01

NUTRITION AND METABOLISM OF DIETARY FAT

This is a study of the human requirements for dietary fat from three perspectives: determination of whole body oxidation of dietary fatty acids by free living subjects, the effect of diet fat on the molecular structure and function of membranes, and determination of neonatal requirements for fat.

Clandinin applies his basic studies to a variety of human problems ranging from the search for an ideal infant formula to the effects of diet on the aging cell. Because diet fat alters the cell membranes, it also affects the metabolism of particular organs. This research has implications for many disease states involving pathological changes in cell membranes.

CODDING, Penelope, Ph.D.*

Assistant Professor

Departments of Chemistry, Pharmacology, and Therapeutics

Faculties of Science and Medicine, The University of Calgary

Date of Appointment: 81/07/01

MOLECULAR STRUCTURE AND FUNCTION STUDIES OF CNS ACTIVE DRUGS AND TOXINS

This is a study of how drugs bind to target molecules which changes their shape and biochemistry. The drug-molecule interaction depends upon the shapes of both drug and receptor molecules and their three-dimensional distribution of reactive groups. Coddling uses X-ray diffraction to identify the three-dimensional shapes of drugs which have similar pharmacological effects and targets. This information is helpful in the development of more effective specifically targeted drugs.

She has developed a research model of the sodium channel receptor site for toxins. Toxins send messages to nerve and muscle cells and cause aberrant electrical properties, for example, in seizures or heart misfirings. She also analyzes synthesized DNA complexed with several anti-cancer drugs to see how the drugs influence DNA biochemistry.

In 1984 Coddling developed 3-D models for two drug systems. She has also identified how structural differences in various anticonvulsants may explain their differing clinical effects and is similarly analyzing drugs used to treat high blood pressure.

DANIELSON, Terry, Ph.D.

Assistant Professor

Faculty of Pharmacy

Department of Pharmacy and Pharmaceutical Sciences
The University of Alberta

Date of Appointment: 81/07/01

METABOLISM AND PLASMA LEVELS OF CLINICAL MONOAMINE OXIDASE INHIBITORS

This is a study of monoxidase inhibitors, drugs used to manage psychiatric illnesses. Though drugs like phenelzine appear to benefit patients, scientists don't know why nor do they understand why often 10 to 14 days of treatment are required before any improvement appears. Danielson is investigating how the body handles phenelzine after acute or chronic dosing by measuring drug levels in animal tissue and in the plasma or urine of psychiatric patients. Differences will be related to the development of antidepressant or toxic responses.

Danielson is also using animal models to investigate new psychoactive substances.

In 1984 Danielson found acetyl-Pz is a potent inhibitor of MAO and began studies comparing Pz and acetyl-Pz. Using an animal model of depression he also found mechanisms of thermic control change when treated with reserpine, an observation that may be fundamental to understanding how antidepressants act.

DASGUPTA, Mrinal, M.D.

Associate Professor

Department of Medicine

Faculty of Medicine, The University of Alberta

Date of Appointment: 82/07/01

MBP SPECIFIC CIC IN MULTIPLE SCLEROSIS

This is a study to establish biological assays to detect immune complexes (IC) in the blood and their relationship to disorders such as lupus, cystic fibrosis and multiple sclerosis (MS). In these autoimmune diseases, the immune complexes (protein antibodies plus disease-producing agents) seem to cause disease rather than fight it. Dasgupta has discovered IC level is important in multiple sclerosis patients. These ICs contain a protein found in the myelin covering of nerve fibres and degradation of this myelin causes the crippling symptoms.

Dasgupta is further investigating specific myelin in the ICs of large numbers of MS patients to see if the ICs could modulate the clinical expression of symptoms. This may lead to new forms of therapy and possibly a vaccine. The same techniques in IC research are also being applied to a form of kidney disease and cystic fibrosis.

In 1984 Dasgupta completed evaluation of over 100 MS patients for immune complexes. He also investigated cystic fibrosis patients with *Pseudomonas aeruginosa* (PA), a chronic lung disease and found they had high levels of antibody to PA and some had circulating immune complexes (CIC). He initiated collaborative research on PA and CIC with investigators in Germany. The Universities of Calgary and Guelph.

DUFF, Henry, M.D.

Associate Professor

Department of Medicine

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

MECHANISTIC APPROACH TO ANTIARRHYTHMIC THERAPY

This is a study of the mechanisms of drug action for drugs

used to treat cardiac diseases. Duff evaluates known drugs, develops new ones, and uses drugs as probes to further understand the basic physiology of the heart. In animal and clinical studies, he particularly investigates antiarrhythmic drugs like quinidine and mexiletine, which are used to control irregular heart rhythms.

In more basic studies, he explores the electrophysiologic changes caused by drugs. This includes a search for specific receptors on heart cell membranes, knowledge which would lead to improved specifically-targeted drugs with less side effects.

In 1984 Duff demonstrated that, in both animal models and human patients, a combination of mexiletine and quinidine was more effective in controlling irregular heart rhythms than doses of either drug alone. He investigated the pharmacokinetics of the therapy and characterized the electrophysiological changes that occur.

FORD, Gordon, M.D.

Associate Professor

Department of Internal Medicine

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

INTERDEPENDENCE OF THE LUNG, RIBCAGE AND DIAPHRAGM DURING ATELECTASIS

This is a study of atelectasis, (areas of lung collapse), which arise from airway disease or accompanying other lung disorders. Atelectasis is particularly common in patients who have had upper abdominal surgery. Ford is investigating the cause of postoperative diaphragm dysfunction and developing experimental therapies.

Once the physiological mechanism is understood and test therapies have proved beneficial, they will be applied to clinical studies for the treatment and possible prevention of atelectasis.

In 1984 Ford used a dog model to identify the reflex pathway(s) responsible for the decreased diaphragm activity seen after gallbladder stimulation. He also studied animals undergoing esophagogastroduodenoscopy to determine how sedation and the effects of the endoscope affected the observed decrease in oxygen saturation seen in patients.

FRANK, Cyril, M.D.*

Assistant Professor

Faculty of Medicine

Department of Surgery, The University of Calgary

Date of Appointment: 84/07/12

CONNECTIVE TISSUE STRUCTURE AND FUNCTION

This is a study of connective tissue properties, primarily ligaments, to understand how they change with maturation, aging, and the healing process. First, Frank is doing a multidisciplinary assessment of normal structure using rabbit models to determine tissue properties. This will be followed by an examination of tissue properties during the natural healing process after injury. The baseline data can then be used to assess treatments such as exercise, immobilization, heat, ice, and ultrasound. Understanding ligament function could advance knowledge of disease such as osteoarthritis and scoliosis. In the

long term, research methods will be applied to other connective tissues such as skin and bone.

In addition to establishing his lab in 1984, Frank initiated a clinical study of knee injury in cooperation with the Community Health Sciences Department at the U of C. He also continues medical practice, specializing in knee surgery.

FRITZLER, Marvin, Ph.D.

Professor and Head Division of Rheumatology and Clinical Immunology

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

ANTINUCLEAR ANTIBODIES: AUTOIMMUNE DISEASES

This is a study of antinuclear antibodies in the serum of patients with autoimmune diseases (diseases where the immune system breaks down and seems to cause disease rather than fight it). Scientists don't understand why unusual antibodies coincide with certain diseases. Fritzler is screening the blood of thousands of donors and follows patients to see if the antibodies are precursors of the disease. He is also using biochemistry techniques to isolate, purify and characterize corresponding nuclear antigens (substances capable of inducing the formation of antibodies).

Fritzler primarily works with antibodies implicated in a very common but mysterious rheumatic disease called systemic lupus erythematosus. In 1984 he identified important correlations between the response of certain antibodies and various forms of lupus. This paves the way for effective diagnosis which is currently almost impossible in early stages of the disease because symptoms are so varied.

Other 1984 studies applied antibody research to autoimmune liver disease and scleroderma.

GILES, Wayne, Ph.D.

Associate Professor

Department of Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/01/01

ELECTROPHYSIOLOGY OF ISOLATED CARDIAC CELLS

This is a study of electrical currents at the level of the single heart cell, a study made possible through a new technique called the voltage clamp method. Giles measures very small currents created by ions moving through a pore or channel in the cell membrane. Thousands of these events are believed to control the pacemaker potential, or ability of the heart to beat spontaneously, and the action potential which triggers and controls the heart's pumping action.

Giles uses the same technology to study the effect of autonomic transmitters and collaborates with clinical researchers in investigating specific effects caused by drugs.

In 1984 Giles and his staff successfully measured the sodium current and related events in single atrial cells. This provides important information for studying the effects of antiarrhythmic drugs. A Fellow in Giles lab, Dr. Shibata, has received widespread

recognition for his measurements of the ionic currents generating spontaneous electrical activity in the pacemaker region of the heart. These findings have been incorporated into a computer simulation of cardiac pacemaker activity.

HANGARTNER, Thomas, Ph.D.
Associate Professor
Department of Applied Sciences in Medicine
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

DUAL ROTATION COMPUTED TOMOGRAPHY SYSTEM FOR BONE AND TISSUE DENSITOMETRY

This is a study of bone disease made possible with a special computed tomography scanner which measures bone density. The scanner enables Hangartner to observe growth and maintenance patterns in the human skeleton. He can determine how bones are affected by hormones, diet, exercise, drugs and other treatments. He is comparing the efficacy of various treatments and has, for instance, found that intermittent drug therapy seems more effective than the traditional prolonged drug intake.

In 1984 Hangartner (in collaboration with Drs. Charles Harley and Tom Overton) conducted a clinical trial with postmenopausal women to evaluate the efficiency of Vitamin D as an activator for bone remodeling cells. The results were significant and they are now continuing research on this and other activators. Procter & Gamble also contracted them to study the influence of phosphate and a diphosphonate on bone.

HANLEY, David, M.D.
Associate Professor
Department of Medicine
Faculty of Medicine, The University of Calgary

Appointment: 81/04/01

PARATHYROID HORMONE (PTH) SECRETION

This is a study of the mediators of parathyroid hormone secretion. PTH is the main regulator of calcium metabolism, a process which is important for normal cell function in all body tissues. This study uses normal animal tissue and abnormal human tissue from patients with parathyroid disease.

Abnormalities of parathyroid function have been noted in many common disease states: kidney stones, chronic renal failure, generalized bone disease such as osteoporosis, and benign tumors of parathyroid glands.

In 1984 Hanley demonstrated two separate cellular pathways for PTH secretion. He also completed the development of a unique radioimmunoassay for PTH and provided the Foothills Hospital and the Calgary General Hospital with a measurement service for PTH. He initiated several ongoing clinical studies of calcium levels related to diseases such as hypertension and nephrolithiasis.

HART, David, Ph.D.
Professor
Department of Microbiology and Infectious Diseases
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/08/22

IMMUNOCHEMICAL CHARACTERIZATION OF PLASMINOGEN ACTIVATORS

This is a study of proteolytic enzymes which play a central role in the regulation of cells and relate to many diseases. For example, uncontrolled enzymes can lead to blood clotting or to the tissue damage that occurs with rheumatoid arthritis.

Hart is investigating a group of enzymes called plasminogen activators which have been associated with cells of the immune system, the hematopoietic system, and tumor cells. He uses animal models to study the enzyme regulation at the cellular and systemic level. Once an information base is established, samples from healthy and diseased tumors will be analyzed in collaboration with rheumatologists and hematologists.

Hart is Chairman of the new Immunological Sciences Research Group at The University of Calgary.

In 1984 Hart acquired important data on how plasminogen activators are regulated by certain monocyte-macrophage cells that play a role in inflammatory processes of many diseases. He also identified a PA inhibitor.

HICKS, Philip, Ph.D.
Assistant Professor
Department of Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

IDENTIFICATION OF SYNAPTIC TRANSMITTERS IN THE MAMMALIAN VISUAL AND SOMATOSENSORY SYSTEMS

This is a study of how visually responsive and somatosensory responsive neurons in the brain communicate via chemical transmitters. Hicks is investigating the chemical mediators, particularly amino acids, to determine their role in processing visual and somatic information. He hypothesizes that different portions of the sensory pathways, which are anatomically segregated and have different functions, are also differentiated by the use of different synaptic transmitters. His investigations are carried out at the level of the single cell using neurochemical, pharmacological and physiological techniques on animal models.

In 1984 Hicks completed three separate studies of synaptic transmitters, including GABA, glutamate and octopamine, and described their synaptic effects central neurons. Other experiments on cat and rat models are ongoing.

HINDSGAUL, Ole, Ph.D.
Assistant Professor
Department of Chemistry
Faculty of Science, The University of Alberta

Date of Appointment: 81/10/01

BIOLOGICAL RECOGNITION OF COMPLEX CARBOHYDRATES

This is a study of how protein receptor-sites specifically recognize complex carbohydrates. The recognition process is a primary step in many body functions such as hormonal regulation, immunological processes, cell recognition and adhesions. Hindsgaul is looking for the molecular description of how the carbohydrates are recognized. He believes the surface of complex

sugars contain discreet, predictable topographical features.

This basic research will lead to more understanding of how the mechanism mediates normal and abnormal body functioning.

In 1984 Hindsgaul synthesized a putative ligatin-receptor important in the recognition process. He also identified the molecular structure of an antigenic determinant of a particular human melanoma cell line, information important in understanding how cell surface carbohydrates may affect tumor development.

HOAR, David, Ph.D.

Associate Professor

Departments of Medical Biochemistry and Pediatrics
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

DNA SEQUENCE DIVERSITY IN MAN

This is a study of DNA sequence changes in relation to specific inherited diseases. Alterations in DNA sequences appear to be very common in humans and appear to arise by a variety of mechanisms. Of the several thousand genetically-inherited diseases, very few have been characterized (the molecular structure identified), to sufficiently identify the basic defect. New molecular biology and recombinant DNA techniques now allow Hoar to identify DNA sequence changes with specific diseases. If he can establish linkage associations, the information could be used for diagnostic studies. In the future, physicians may be able to precisely predict who will inherit certain diseases, an important step towards prevention.

In 1984 Hoar identified and cloned a number of DNA sequences to identify specific genes. He continues to investigate the genetic factors involved in chromosomal nondisjunction which leads to retarded babies. He also analyzes human viruses in blood products and has developed potentially valuable ways of diagnosing viruses in the lab.

HOFFER, Andy, Ph.D.

Associate Professor

Departments of Medical Physiology and Clinical
Neurosciences

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/11/05

NEURAL CONTROL OF MOVEMENTS

This research program focusses on how neural function controls muscle contraction leading to voluntary movement. Hoffer records electrical currents in single, specifically-identified nerve cells in the spinal cord during normal animal movement. This is possible because of recently developed recording devices which are surgically implanted. Hoffer is studying three aspects: the "language" of motor neurons, the electrical activity of sensory nerve fibers bringing information from the muscles to the central nervous system, and the communication between the spinal cord segments and higher levels of the brain.

Hoffer's implantable interfaces with nerve and muscle have already found clinical application in the control of prosthetic limbs in amputees. This research may also become relevant to the development of new therapies and diagnostic procedures for neurological disorders like Parkinson's Disease.

In 1984 Hoffer and his collaborators developed the methodology to record, for the first time ever, the natural activity patterns of identified spinal cord neurons in intact, freely moving animals. He initiated investigations on: the spinocerebellar tract neurons, the development of sensory signals from the lungs in fetal lambs (to study respiration control during birth), and the role of motoneurons and muscle afferents in the control of normal posture.

HULBERT, William Ph.D.*

Assistant Professor

Department of Medicine

Faculty of Medicine, The University of Alberta

Date of Appointment: 84/07/01

THE EFFECT OF H₂S ON AIRWAY STRUCTURE AND FUNCTION

This is a study of airway injury caused by sour gas using the guinea pig as an animal model. Hulbert uses light microscopy and scanning electron microscopy to assess how breathing H₂S affects the cellular structure of airway and lung cells. Hulbert will examine the mechanism of the knockdown effect, the results of graded doses of H₂S and eventually the dynamics of repair following sour gas injury.

IATROU, Kostas, Ph.D.

Associate Professor

Department of Medical Biochemistry

Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

THE ORGANIZATION, EXPRESSION AND EVOLUTION OF EUKARYOTIC MULTIGENE FAMILIES IN CHORION OF BOMBYX MORI

This is a study of mechanisms regulating differential gene expression which results in normal or abnormal cellular differentiation and development. The chorion (eggshell) of the silkworm is used as a model system because it is composed of many distinct proteins encoded by a large number of genes whose expression is developmentally regulated according to a strict temporal program. Wild type and mutant silkworm strains are used for the analysis of the molecular organization of chorion genes expressed at different stages of oogenesis. Iatrou is identifying elements that may be involved in the control of chorion gene activation, and testing regulatory models of different gene activity.

An in-depth understanding of gene regulation at the molecular level is an essential prerequisite to the understanding of normal and abnormal cellular behavior and to the eventual treatment of disorders of cell differentiation and development, such as genetic defects and cancer.

In 1984 Iatrou initiated the development of functional assay systems for measuring transcriptional activities of cloned chorion genes in homologous and heterologous cells in culture and in live animals. He also engineered the genetic information of an insect virus in a way that allowed him to produce foreign gene products in insect tissue culture cells under the control of viral regulatory elements.

JARVIS, Simon, Ph.D.
Associate Professor
Department of Physiology
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/08/01

MOLECULAR PROPERTIES AND REGULATION OF THE NUCLEOSIDE TRANSPORT SYSTEM

This is a study of nucleosides, agents used in the treatment of viral and neoplastic diseases. Because the agents (nucleoside analogs) enter cells through a saturable transport mechanism in the cell membrane, the transportability of an analog is an important determinant of its biological activity. Jarvis is investigating the molecular basis of nucleoside transport using a high-affinity nucleoside transport inhibitor. Once the membrane components are identified, he will examine the regulation and synthesis of nucleoside transport protein.

This study has direct relevance to viral and cancer chemotherapy.

In 1984 Jarvis clearly identified a particular polypeptide as the nucleoside transporter in human erythrocytes (red blood cells) and found the molecular weight of the nucleoside transporter in other animal cells was similar. With the molecular properties of the nucleoside transport system he has identified so far, Jarvis is now ready to investigate nucleoside transporters in malignant cells.

JAWORSKI, Martine, M.D.
Associate Professor
Department of Pediatrics
Faculty of Medicine, The University of Alberta

Date of Appointment: 83/07/01

PATHOGENESIS OF INSULIN DEPENDENT DIABETES MELLITUS

This is a study of juvenile-onset insulin-dependent diabetes. Scientists now believe genetically predisposed individuals may acquire diabetes through a complex interaction between an outside event such as a viral infection and the response of the person's immune system. Jaworski is investigating the genetic susceptibility and the autoimmunity (where cells in the immune system cause rather than prevent disease) of juvenile diabetes. She compares the immunoregulation of diabetics, their close family members, and normal individuals. So far, studies indicate the diabetic child may have an imbalance of helper and suppressor cells in his or her immune system.

In 1984 Jaworski found cyclosporin induced complete and long-term protection against diabetes in diabetes-prone BB rats. Paradoxically, it also induced the development of the disease in low-risk (diabetes-resistant) BB rats; the mechanism by which it might do so, (either directly through the killing of beta cells, or indirectly by shifting the balance in the immune system) is currently being examined. Jaworski's studies strongly suggest cell-mediated autoimmunity is an important contributor to the development of the disease.

Jaworski also established a bank of serum and HLA typed lymphocytes from diabetics and control individuals to facilitate clinical research. She is collaborating with others to establish specific tests to predict the disease in high-risk individuals, and to monitor diabetics on immunotherapy.

JENSEN, Susan, Ph.D.
Associate Professor
Department of Microbiology
Faculty of Science, The University of Alberta

Date of Appointment: 81/07/01

BIOSYNTHESIS OF NOVEL PENICILLIN AND CEPHALOSPORIN ANTIBIOTICS

This is a study of the natural production of penicillin and cephalosporin antibiotics by the organism *Streptomyces clavuligerus*. DNA technology is used to increase the production of the *Streptomyces clavuligerus* enzymes which synthesize the antibiotics. If these enzymes can be harnessed as biological catalysts (in cell-free systems) to synthesize many antibiotics, the expensive chemical modifications currently used to enhance antibiotics will be unnecessary. This means more effective and reasonably-priced antibiotics.

In 1984 Jensen and her colleagues, Dr. Saul Wolfe of Queen's and Dr. Donald Westlake also from the U of A, successfully produced a number of penicillin and cephalosporin antibiotics using the cell-free enzymatic system. One of the substrate analogues is especially promising because its products have good antibacterial properties in comparison to a widely used cephalosporin and it appears to be readily absorbed orally, a major disadvantage of many third generation cephalosporins.

KAUFMAN, Susan, Ph.D.
Associate Professor
Department of Medicine
Faculty of Medicine, The University of Alberta

Date of Appointment: 83/04/01

CONTROL MECHANISMS OF FLUID AND ELECTROLYTE BALANCE

This is a study of how the body controls intake and output of salt and water, factors pertinent to many disease states, particularly hypertension and congestive heart failure. To control salt and water, the body needs a mechanism for measuring fluid volume and salt content. Kaufman uses animal models to investigate volume sensors in the heart. She is investigating whether signals from the volume sensors are transmitted directly to the brain or whether they cause hormonal changes which alter thirst, salt appetite and urine output.

Preliminary research by Kaufman and others indicates there might be such a hormone originating from the heart. She is specifically applying the principle to studies of congestive heart failure.

In 1984 Kaufman demonstrated that stretching the right atrium with a balloon significantly reduces the natriuretic activity of extract prepared from tissues. She also showed that the right atrial receptors influence thirst and salt appetite in rats.

KOOPMANS, Henry, Ph.D.
Associate Professor
Department of Medical Physiology GI Research Group
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/08/22

THE INTERNAL CONTROL OF FOOD INTAKE

This physiological study of food intake is directed toward discovering a new medical treatment for obesity. Koopmans' previous work indicates there are two types of signals that inhibit food intake: a hormone released from the stomach inhibits short-term intake and a signal, probably a hormone, arising in the lower small intestine reduces long-term intake. Using animal models, Koopmans is investigating the chemical nature of these signals, the food that release them and the way they affect the brain.

Since obesity increases the risk of many debilitating illnesses such as diabetes, stroke, and heart disease, this research has widespread relevance.

In 1984, Koopmans completed several experiments on crossed intestines rats which showed that absorbed food has a major effect on the long-term control of food intake and overrules short-term signals from the stomach. He also developed an animal model for patients with kidney failure who are on chronic dialysis and will continue to examine how diet affects this condition.

LAU, David, M.D.*

Assistant Professor

Department of Medicine

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/07/12

REGULATION OF ADIPOSE TISSUE DEVELOPMENT AND GROWTH

This is a study of obesity at the cellular level. Lau is investigating the development and growth of adipose (fat) tissue by exploring the interplay between adipose and capillary endothelial cells (cells lining the inside walls of small blood vessels). Previous research by Lau and others indicates the anterior pituitary gland releases novel proteins that act as adipocyte growth factors.

In search of more novel adipocyte growth factors, Lau compares the growth, structure, and biochemistry of capillary endothelial cells from diabetics, obese, and healthy persons of normal weight. This research is also relevant to the understanding of such diabetic complications involving capillary blood vessels as retinopathy, a leading cause of blindness in diabetics.

Lau is also founding director of The Foothills Hospital Outpatient Lipidemia and Weight Control Clinics. The latter offers patients a 12 week multidisciplinary program.

LEE, Patrick, Ph.D.

Assistant Professor

Department of Microbiology and Infectious Diseases

Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

THE MECHANISM OF VIRUS ATTACHMENT ONTO HOST CELLS

This is a study of the first step in viral invasion—the way a virus attaches to the host cells. The reovirus (REO, respiratory enteric orphan) found in the human digestive tract is a valuable research model because the virus cell attachment apparatus (protein sigma 1) has been identified and the viral gene that codes for this attachment protein is easily isolated.

It is believed that the virus gains entry into the host cell by first anchoring itself via the attachment protein sigma 1 onto specific

"receptors" on the host cell membrane. Using monoclonal antibody production and genetic engineering, Lee is investigating the biochemical nature of the virus attachment apparatus and the cellular receptor. Understanding the process is a step in the development of antiviral measures designed to block cell-virus interactions at the plasma membrane level.

In 1984 Lee became the first to publish the reovirus S1 gene sequence. He made continued progress towards getting the gene to express the functional cell attachment protein. He also identified the reovirus receptor on the target cell.

LEFEBVRE, Yvonne, Ph.D.

Associate Professor

Department of Medical Biochemistry

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

PASSAGE OF STEROID AND THYROID HORMONES ACROSS THE NUCLEAR ENVELOPE OF MAMMALIAN CELLS

This is a study of why some breast carcinomas are unresponsive to steroid hormone treatment. Currently hormone manipulation causes regression in about 25 percent of breast carcinomas. Because steroid hormones interact with the gene, they must enter the nucleus via a double membrane system, the nuclear envelope which forms a barrier between cytoplasm and nucleus.

Lefebvre hypothesizes passage across this nuclear envelope may be defective in unresponsive tumors. She is investigating the molecular mechanisms by which steroids traverse the nuclear envelope of normal mammalian target and non-target cells, as well as steroid-responsive and steroid-unresponsive neoplastic cells.

In 1984, while on sabbatical at the Cancer Control Agency in Vancouver, Lefebvre helped successfully conclude a twenty-year attempt to purify the nuclear androgen receptor. The availability of purified receptors will make it possible to conduct a whole new series of experiments investigating cell responses to cancer treatment.

LEUNG, Wai-Choi, Ph.D.

Associate Professor

Departments of Medicine and Infectious Diseases

Faculty of Medicine, The University of Alberta

Date of Appointment: 82/07/01

MOLECULAR CLONING OF VIRAL NEUTRALIZATION ANTIGEN AND HUMAN TUMOR ANTIGEN

This is a study of ways to use molecular genetic technology to produce effective vaccines for virus-induced diseases. Experimental vaccines recently developed for herpes simplex virus and influenza virus seem effective. However, the minute amounts of neutralization antigen that can be isolated from purified virus prevents large-scale production of the vaccines. Leung is mass producing the virus neutralization antigens in genetically-engineered microorganisms which should reduce production costs and possible hazards.

A second project focuses on the molecular cloning of an antigen associated with human melanoma (pigment-bearing malignant tumors).

In 1984 Leung completed the first steps towards producing the neutralization antigen of the herpes simplex virus by molecularly cloning key structural genes for glycoproteins.

He also developed antibodies against specific peptides on predicted antigenic sites for one glycoprotein. These advances provide the base necessary to eventually develop a vaccine against the disease.

LORD, Catherine, Ph.D.*

Associate Professor

Department of Pediatrics

Faculty of Medicine, The University of Alberta

Date of Appointment: 84/07/01

SEX DIFFERENCES IN AUTISM

This is a descriptive study of the cognitive, behavioral and medical characteristics of males and females with autism. Conducted in collaboration with scientists in the United States and Britain, the study includes subjects of normal intelligence or mild retardation. The project will describe patterns of skills and deficiencies of females compared to males and differentiate language, social and cognitive skills of high-functioning persons.

This information will yield valuable clues to the possible neurological and genetic causes of autism and help identify treatment goals.

MacVICAR, Brian, Ph.D.

Assistant Professor

Department of Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 83/04/01

NEURONAL BASIS FOR SYNCHRONY DURING SEIZURE

This is a study of brain seizures, particularly epileptic seizures which frequently start in the hippocampus. Seizures are believed to be caused by sudden, abnormally large excitation of a large group of nerve cells. MacVicar is investigating why the cells in the hippocampus fire simultaneously and how they are interconnected.

New technology allows MacVicar to record the cellular activity of live nerve cells as they are affected by convulsants (agents which induce seizures). Animal models are used for this research.

In 1984 MacVicar discovered a new role for a type of brain cell called a glial cell. Glial cells were thought to be silent, supporting brain cells but he discovered glial cells in culture are electrically excitable. If this is true of cells under typical conditions in the brain, malfunction of the glial cell system might explain electrical hyperactivity occurring during seizures.

MANNONI, Patrice, M.D.

Associate Professor

Department of Pathology

Faculty of Medicine, The University of Alberta

Date of Appointment: 82/10/01

ANTIGEN CHARACTERISTICS OF HEMATOPOIETIC STEM CELLS

This is a study of how normal and leukemic blood cells differ in development and structure. Mannoni studies surface membrane markers using monoclonal antibodies produced in vitro by mouse

cells immunized against leukemia or normal cells and infused with tumor cell lines. Cell culture techniques allow him to study the possible expression of these markers during normal and leukemic cell proliferation. Mannoni is looking for oncogenes, little understood genes which some scientists believe may undergo change when cancer occurs, or which may be caused by the cancer. The project also includes an investigation of how the membrane markers are modified by external agents such as interferon.

In 1984 Mannoni identified a number of cell surface markers which may be receptors (signals) for the control of cell proliferation and/or differentiation. In collaboration with others, he established some growth factors could induce differentiation of normal and leukemic cells.

MARANDA, Bruno, Ph.D.

Assistant Professor

Department of Surgery

Faculty of Medicine, The University of Alberta

Date of Appointment: 83/05/17

IMMUNO-CYTOCHEMICAL INVESTIGATION OF AXONAL TRANSPORT

This is a study of the movement of materials from cell centre to nerve terminals and back via axons. Maranda is investigating the chemical nature of membrane-bounded particles which are transported in the axons and he is identifying the cytoskeletal structures involved. He uses conventional and monoclonal antibodies in conjunction with video-enhanced microscopy. Amplifiers and a television camera create a system sensitive enough to observe how fluorescently-labelled particles move through living axons.

Better understanding of axonal transport will lead to more information about neurological diseases, particularly those involving degeneration of peripheral nerves.

In 1984 Maranda used the giant axons of American lobster walking legs to demonstrate organelles moved through microtubules and that axonal transport is not a passive flow as many have suggested, but an active process.

MARTIN, Renée, Ph.D.*

Associate Professor

Department of Pediatrics

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/07/01

CYTOGENETIC ANALYSIS OF HUMAN SPERM

This is a study of chromosomal abnormalities in human sperm using a new technique that activates the sperm so that they can be visualized. Chromosomal abnormalities are a significant cause of birth defects and mental retardation.

Martin is investigating a normal control population to establish the distribution and variation in the frequency of abnormalities to determine whether some men are at increased risk. Factors studied include radiotherapy for treatment of cancer, age, and whether all chromosomes are equally susceptible to error. Investigations on the possibility of sperm selection (based on chromosome constitution) in humans and other basic studies will also yield new information on the causes of birth defects.

MATHESON, David, M.D.
Associate Professor
Department of Pediatrics and Internal Medicine
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

CELLULAR REGULATION OF IMMUNE RESPONSES

This is a study of how interferon affects natural killer (NK) cells. These white cells have a special ability to kill other cells that have been infected by a virus or become malignant and their activity varies according to naturally occurring factors or drugs. Several patients with cancer have markedly depressed NK activity, but it is not known if this is cause or effect.

Matheson is testing the effects of two types of interferon on NK, as well as other immune functions, and he has found in some patients interferon leads to decrease in NK. He is also investigating how some drugs influence DNA metabolism and how changes in the DNA building blocks affect the level of NK activity.

In 1984 Matheson identified a number of drugs that modulate the immune system favorably or unfavorably. He found D-glucosamine and aminoglutethimide markedly increase NK cell activity in cancer patients. A suppressive effect is induced by two major cardiac drugs. Chronic treatments for certain diseases can also suppress activity. Matheson found the immune system of some hemophiliacs is sensitized to the product they take to counteract bleeding.

McFADDEN, Grant, Ph.D.
Associate Professor
Department of Biochemistry
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

MOLECULAR BIOLOGY OF TUMORIGENIC SHOPE FIBROMA POXVIRUSES

This is a study of the molecular interplay between one particular tumor-promoting virus, the poxvirus in rabbits, and its target cell. This virus is the only DNA tumor virus which does not exert its effect from a location in the cell nucleus. It can be studied in tissue culture cells grown in the lab.

McFadden is attempting to dissect out the viral genes responsible for the virus's oncogenic potential and to analyze those genes using recombinant DNA cloning and DNA-mediated gene transfer. Since the poxvirus has never been systemically studied at the molecular level before, this research may clarify how a mammalian cell transforms itself into an unregulated and rapidly-dividing tumor cell.

In 1984 McFadden completed a long series of experiments designed to clone certain fragments of the Shope fibroma virus (SFV) and to map six key restriction enzyme sites, a key step in understanding tumorigenesis. He also acquired critical information on the genome of a related poxvirus, malignant rabbit virus. A Fellow, Dr. Chris Upton, acquired evidence that suggests a plasmid species may mediate an exchange of genetic information between SFV and the target rabbit cell.

MILLER, Rodman, Ph.D.
Assistant Professor
Department of Anatomy
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/10/01

FREEZE FRACTURE LOCALIZATION OF ANTIGENS AND OF CHOLESTEROL

This is a study of the development of freeze fracture techniques to identify specific structures in membranes; currently the technique, called freeze fracture electron microscopy, yields a picture of individual proteins as particles imbedded in a (fracture) biological membrane. However, it has not been possible to associate a size or shape of a membrane particle with a particular protein. Miller is developing a technique which uses dyes bound to biologically active materials and an argon laser to selectively heat regions of the membrane. The procedure should allow scientists to specify the molecular identity of objects seen through freeze fracture.

This technique will have many applications in medical research because investigators will be able to locate membrane receptors in a variety of tissues. Miller will apply the method to locate neurotransmitter receptor cells in the retina.

In 1984 Miller found evidence that suggests cholesterol is assymmetrically distributed in most biological membranes. He also continued collaborative work on the morphological changes of membranes in muscular dystrophies.

MILOS, Nadine, Ph.D.
Assistant Professor
Department of Anatomy
Faculty of Medicine, The University of Alberta

Date of Appointment: 83/09/01

FACTORS CONTROLLING PATTERN FORMATION BY NEURAL CREST CELLS

This is a study of the mechanisms which control the arrangement and pattern of cells. Scientists don't understand how individual cells come together to form a functional group such as an organ. Using neural crest cells of a species of toad, Milos is studying cellular pattern formation at the earliest embryonic stages of development.

Milos believes the cells may communicate with one another via a chemical gradient of diffusible molecules which enables them to locate their positions in relation to other cells and shift position. She hopes to isolate and characterize the biochemical components forming this gradient as well as identify any relevant changes in cell surface properties.

Understanding this mechanism will lead to more knowledge about inappropriate cellular combinations that occur in congenital defects or in the development of tumors with subsequent metastasis.

In 1984 Milos developed an experimental system to test for putative diffusible molecules involved in neural crest formations. Early results indicate that these types of molecules and cell surface carbohydrates play a role.

MINUK, Gerald, M.D.
Assistant Professor
Department of Medicine
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/07/01

ROLE OF GABA IN LIVER DISEASE

This is a study of γ -aminobutyric acid (GABA), a potent amino acid neurotransmitter that has been implicated as a cause of certain features of liver disease. Normally GABA produced elsewhere in the body is metabolized by the liver or secreted into the bile duct drainage system but Minuk has discovered some GABA remains in the liver where it presumably carries out certain functions. His preliminary investigation of these functions indicates that they may be involved with normal bile flow or changes in insulin and glucagon effects on the liver. Abnormal metabolism of GABA by the liver appears to play a role in the suppression of normal brain activity that is seen with severe liver disease.

Understanding the physiology of GABA will give insight into why people with severe liver disease develop metabolic abnormalities and occasionally coma.

In 1984 Minuk completed two clinical studies, one on advanced liver disease and hepatic encephalopathy and one on the serum of young children who had died of Reye's syndrome, a disease affecting the liver and central nervous system. Results strongly indicate GABA plays a role in the pathogenesis of hepatic encephalopathy in adults and children. Minuk's animal research focused on how certain drugs used to treat liver disease affect GABA levels.

MOORE, Graham, Ph.D.
Associate Professor
Department of Medicine
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

THE SYNTHESIS AND EVALUATION OF PEPTIDE HORMONES AND ANALOGUES

This is a study of how two peptides, angiotensin and vasopressin, function in normal and abnormal states. Because both of these peptides are involved in hypertension and heart failure, Moore is searching for ways to eliminate their undesirable effects in cardiovascular diseases. He is studying the biosynthetic pathways which give rise to the peptides and how they act at their tissue receptors.

This information prepares the way for synthesizing peptides which correct the negative action and could then be incorporated into drugs for the diagnosis and treatment of heart failure.

In 1984 Moore synthesized the first cyclic angiotensin antagonist which opens new opportunities to manufacture hypertension drugs. He also synthesized a new type of angiotensin antagonist and four international companies are currently investigating one of the relevant peptides.

MORTIMER, David, Ph.D.
Assistant Professor
Department of Obstetrics & Gynecology
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/10/01

HUMAN SPERM PHYSIOLOGY AND INFERTILITY

This is a study of male fertility designed to develop more effective treatments of involuntary infertility. While understanding of female infertility and treatment is well advanced, little is understood about male fertility so there are no reliable tests to assess fertility potential and few, if any, useful therapies. Mortimer is investigating sperm physiology, specifically the dynamics controlling the ascent of the spermatozoa through the female reproductive tract to the site of fertilization and their interaction with eggs. He is also establishing techniques for assessing the competence of human spermatozoa. These techniques will be applied to investigate infertile couples at The University of Calgary Infertility Clinic where Mortimer is Director of the Semiology Laboratory.

Mortimer's research may lead to more effective infertility therapies (for example treatment which enables subfertile men to fertilize human eggs in vitro) and may also suggest new approaches for contraceptive techniques.

In 1984 Mortimer established a diagnostic semen laboratory to provide state-of-the-art semen analysis and screening services at the U of C Endocrine/Infertility Clinic. He also developed a new culture medium that maintains the mobility of human spermatozoa.

NORTHUP, John, Ph.D.
Assistant Professor
Department of Pharmacology and Therapeutics
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/05/12

GTP BINDING PROTEINS AND ADENYLATE CYCLASE

This is a study of the second messenger system, known as cyclic AMP, which mediates the cellular actions of many important hormones. For example, by activating different specific enzymes inside cells, the same second messenger system causes the liver to produce glucose and the heart to increase its rate of beating in response to the hormone epinephrine.

Northup is investigating how hormones regulate adenylate cyclase, the enzyme which synthesizes cAMP. He has purified two GTP-binding proteins which are responsible for "coupling" hormone receptors with adenylate cyclase and are similar to another GTP-binding protein that mediates the visual response of the black and white vision cells. Since these structurally similar proteins appear to be part of a family, Northup hopes to determine if there are other similar proteins and to identify the transmembrane signalling processes they mediate. He has already identified an additional GTP-binding protein of unknown function and has found a different form of the common subunit.

Understanding the biochemistry of the regulating proteins will lead to more knowledge of how many disease conditions occur, and will eventually open new possibilities for drug therapy.

In 1984 Northup modified a technique for large scale preparation of two proteins in animals. This prepares the way for characterizing the proteins in humans with a potential for diagnosing endocrine diseases. He also found beta unit function for three proteins appears to be highly conserved, providing strong evidence of ubiquitous beta subunit among GTP-binding regulatory proteins.

PALCIC, Monica, Ph.D.*

Assistant Professor

Department of Food Science

Faculty of Agriculture/Forestry, The University of Alberta

Date of Appointment: 84/08/01

ENZYME INHIBITORS AS THERAPEUTIC AGENTS

This is a biochemical study of an enzyme called monoamine oxidase (MAO) which acts as a catalyst in the metabolism of neurotransmitters in the brain. Many antidepressant drugs are based on their ability to inhibit MAO and though effective, cause toxic side reactions, sometimes related to food-drug incompatibilities.

Palcic is investigating the biochemical difference between two forms of MAO, particularly their respective binding sites. This kind of information would allow researchers to develop new selectively-targeted drugs free of side reaction.

PARHAD, Irma, M.D.*

Assistant Professor

Departments of Pathology and Clinical Neurosciences

Faculty of Medicine, The University of Calgary

Date of Appointment: 84/07/11

NEUROFIBRILLARY DEGENERATION: PATHOGENIC MECHANISMS

This study examines synthesis, axonal transport and metabolism of neurofilaments and other cytoskeletal components in toxic models (IDPN, aluminum, doxorubicin) of neurofibrillary degeneration. Neurofibrillary degeneration is a hallmark of many human degenerative disorders of the central nervous system such as Alzheimer's Disease, Parkinsonism, and aging.

Parhad has also established a Dementia Clinic at the U of C as a centre for diagnostic services, patient care, and clinical research.

PARSONS, Howard, M.D.

Associate Professor

Department of Pediatrics

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/01

ABSORPTION AND METABOLISM OF LONG CHAIN FATTY ACIDS

This is a study of how nonessential fatty acids affect the absorption and utilization of linoleic acid. Linoleic acid is the major essential fatty acid which, like other essential fatty acids, cannot be synthesized by humans and must come from food. It is necessary for growth, normal cell function and other body processes.

Linoleic acid is one of three fatty acids in the oral triacylglycerals usually given to people with essential fatty acid deficiency, but scientists don't know how the nonessential fatty acids affect the essential ones.

In 1984 Parsons examined essential fatty acid deficiency in cystic fibrosis patients and evaluated two new therapies. Other projects included analysis of nutrients in four meat-base infant formulas and a comparative study of two methods to measure energy expenditure in the surgical/trauma patient. He continues basic research on long-chain fatty acids and provides specialized counselling for nutritional and metabolic disorders in patients throughout the province, particularly infants.

PREIKSAITIS, Jutta, M.D.

Assistant Professor

Department of Medicine

Faculty of Medicine, The University of Alberta

Date of Appointment: 83/07/01

TRANSFUSION ACQUIRED CYTOMEGALOVIRUS INFECTION: Epidemiology and Immune Response in Man

This is a study of cytomegalovirus (CMV) infection which occurs in many forms including a newborn infant infection and an adult disease similar to infectious mononucleosis. Its most serious form occurs in organ transplant patients and may lead to death.

CMV has been associated with blood transfusion. Half of all donor blood units contain antibodies to CMV and therefore have the potential to transmit the infection. Latent cytomegalovirus in blood products appears to reactivate and infect some patients and not others. Preiksaitis is examining the patient-related and the blood product-related factors which allow this reactivation of CMV and its transmission by blood transfusion.

Hopefully, this work will lead to new programs for prevention based on screening blood products for CMV antibodies and on new understanding of the recipient's immune system.

In 1984 Preiksaitis screened over 5,000 transfusion recipients for antibodies to CMV and followed 289 patients seronegative for CMV prior to transfusion. She found the overall low incidence of infection prevented analysis of differences in risk in patient populations. A second study focussed on CMV infection in renal transplant patients and demonstrated 100% transmission of CMV from seropositive organ donors to seronegative patients resulting in infection but not graft loss.

QUANDT, Fred, Ph.D.

Assistant Professor

Department of Medical Physiology

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/08/12

ELECTRICAL PROPERTIES OF ISOLATED RETINAL NEURONS

This is a study of the processes which generate electrical signals in neurons. Complex electrical activity in neurons is generated by membrane pores which open in response to various stimuli including transmembrane voltage and neurotransmitters. Quandt measures electrical currents caused by ion flow through pores in a small patch of neuronal membrane. He is working towards theory which will explain the chemical reactions underlying the operation of those pores.

This basic research will help scientists understand diseases of the nervous system such as epilepsy, dementia, congenital disorders, and psychiatric disorders.

In 1984 Quandt completed the identification of outward currents recorded from membranes of glial cells in rat brains. He acquired evidence that glial cells possess a calcium-activated K channel similar to those in neurons and secretory cells.

RAMCHARAN, Savitri, M.D., Ph.D.*

Professor

Department of Community Health Sciences
Faculty of Medicine, The University of Calgary

Date of Appointment: 84/10/09

EPIDEMIOLOGIC STUDIES OF THE MENSTRUAL CYCLE AND PMS

This is an epidemiological study to measure the frequency and degree, in a 24-hour period, of a wide variety of symptoms and experiences indicative of well being or sickness in women during their child-bearing years. Ramcharan is surveying 7,500 Canadian women to obtain unbiased, population-based information that will enable her to explore the relationship between these factors and certain medical history, personal or life-style characteristics of the women. The goal of the study is to determine if there are differences in women at different stages of their reproductive life, that is, in pregnancy, the post-partum period, phases of the menstrual cycle, oral contraceptive-induced cycle, or perimenopause. The findings are expected to help clarify the relation of certain symptoms to menstrual cycle changes, comprising what is known as the premenstrual syndrome (PMS). Though there are many hypothesis about the disease, research has been hampered by lack of a precise definition of the condition and of objective methods of measurement, and by diagnostic bias arising from the preconceptions of women and physicians.

The survey data will provide a population distribution of menstrual cycle days which will be used as the standard of comparison for analysis in the second stage of research. In this stage a series of case-control studies will determine if women in the premenstruum are more prone to accidents, acute illness, or disorderly behavior than women at other phases of the menstrual cycle. This research will help to clarify the condition and prepare the way for further investigation into the nature and treatment of PMS.

RATTNER, Jerome, Ph.D.

Associate Professor

Departments of Medical Biochemistry and Anatomy
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/10/07

HIGH ORDER STRUCTURE OF CHROMOSOMES

This is a structural study of the organization of chromatic fibers in both the active and inactive state. The basic chromatin fiber is composed of a linear array of "tuna can" shaped subunits called nucleosomes linked by DNA. Each nucleosome is composed of DNA combined with a group of proteins called histones. Rattner is studying how the organization of the basic chromatin fiber changes during transcription and replication as well as how the fiber is "folded" to form higher order structures (chromosomes) during the cell cycle.

This research is part of many studies directed towards understanding normal cell functions as a step to understanding disease processes.

In 1984 Rattner conducted a number of studies that revealed that both helical and loop chromatin packing arrangements co-exist within metaphase chromosomes. These observations provided the basis for the proposal of a new model of chromosome structure. The relationship between chromatin packing hierarchies suggested by this model provides a basis for understanding the structural organization of many cytogenetic abnormalities.

REH, Thomas, Ph.D.*

Assistant Professor

Department of Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 84/09/01

REGENERATION OF OPTIC NERVE

This is a study of nerve regeneration using the retinotectal project of the frog as a model for the study of neural map formation. When the frog's optic nerve is damaged it regenerates and somehow axons manage to find the right place to reconnect so that images from the retina continue to be relayed to the brain.

Reh suspects an electrical interaction is involved and he uses electrophysiological techniques to identify how spontaneous discharge of electricity in the optic nerve correlates with neighboring nerve cells. If he can understand the frog model he will have a clue to the general process of nerve regeneration which could eventually lead to new therapies for damaged nerves.

REHA-KRANTZ, Linda, Ph.D.

Assistant Professor

Department of Genetics
Faculty of Science, The University of Alberta

Date of Appointment: 81/01/01

THE BIOCHEMICAL BASIS OF MUTATION

This is a study of DNA polymerase, the key enzymes in DNA replication. The bacteria-destroying virus called Bacteriophage T4 provides an ideal research model because DNA polymerase mutants can be isolated and the mutant T4 polymerases can be purified. Mutator DNA polymerases no longer replicate DNA accurately and Reha-Krantz is studying them to learn more about the molecular mechanisms controlling accurate and inaccurate DNA replication. Each time a cell reproduces, it is essential that the genetic information (DNA) be copied accurately.

Increased spontaneous mutation rates have been observed in tumor cells. Therefore, though this basic genetic study potentially has wide applications, it is particularly relevant to understanding carcinogenesis.

In 1984 Reha-Krantz completed isolating a number of novel DNA polymerase mutants with mutation frequencies several thousand-fold above wild type levels and has determined the types of mutations produced. Three polymerases have also been purified. This provides tools to determine the molecular defect that causes inaccurate DNA synthesis.

REYNOLDS, John, Ph.D.
Assistant Professor
Department of Medical Physiology
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/10/11

STUDIES OF THE INTESTINAL IMMUNE SYSTEM

This is a study of how the intestinal immune system develops and functions. Reynolds collects the lymphoid cells of sheep as they are transported in the lymph from the wall of the intestine and investigates their origin, pattern of migration and maturation, and microorganisms which may influence them. He uses the same animal model to study how the system develops during the transition from the intrauterine environment (which is free from pathogens) to the postnatal environment where there are many pathogens.

Reynolds' other project on Peyer's patches (large accumulation of lymphoid cells found along the intestinal tract), should lead to a better understanding of B lymphocytes, which are precursors of cells that secrete antibodies to provide immunity against many diseases.

In 1984 Reynolds accumulated evidence that B cell proliferation is independent of antigen and under endogenous control. He also established that final maturation of B cells to plasma cells can start in the Peyer's patches.

RORSTAD, Otto, M.D., Ph.D.
Associate Professor
Department of Medicine
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

MECHANISMS OF ACTION OF BRAIN PEPTIDES

This is a study of brain peptides, substances which scientists believe act as chemical messengers between brain cells and probably cells in other organs. Rorstad is investigating the biochemical mechanisms of peptide function in the pituitary gland (SRIF) and vasoactive intestinal polypeptide (VIP) using a number of animal research models including cloned cells from pituitary tumors.

Peptide research is of great interest to all investigators because they suspect peptides may be involved in many disorders of the nervous and endocrine system.

In 1984 Rorstad acquired evidence indicating that the entire neuropeptide VIP is required for full biological activity. Other studies suggest mechanistic coupling of the cerebrovascular receptors for VIP and PTH to the enzyme adenylate cyclase.

SEVERSON, David, Ph.D.
Associate Professor
Department of Pharmacology & Therapeutics
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

REGULATION OF LIPID METABOLISM

This is a study of lipids, substances in the body which are an important source of oxidative energy in cells and which play a role

in diseases like atherosclerosis. Severson is investigating factors which control lipid metabolism. If he can identify metabolic interventions that would decrease lipid activity in heart tissue deprived of oxygen, new therapies could be developed to reduce damage following a heart attack.

He is also studying lipid metabolizing enzymes in arterial tissue to understand the biochemistry of atherosclerosis. Once enzyme regulation is understood, scientists may be able to retard the build-up of plaque deposits which clog the arteries.

In 1984 Severson completed a study on phosphatidylcholine biosynthesis. In studies of cardiac metabolism he demonstrated lipolysis occurs in myocardial cells at a rate accelerated by hormones. Related work focused on myocardial lipolysis of the diabetic heart. Severson also investigated proliferation of arterial smooth muscle cells, an event that can lead to atherosclerosis.

SINGH, Bhagirath, Ph.D.*
Associate Professor
Department of Immunology
Faculty of Medicine, The University of Alberta

Date of Appointment: 85/01/01

MECHANISM & REGULATION OF ANTIGEN RECOGNITION BY T-LYMPHOCYTES

This is the study of how T cells recognize foreign antigens to activate the body's natural immune system and fight disease. Singh studies the interaction between T cells and foreign antigens with three protein models: a synthetic peptide called poly 18, the cytochrome C molecule and insulin molecule. He has characterized a gene for the T cell receptor from the insulin reactive T cells.

Singh investigates transplantation antigens which are central to understanding how the immune system combats disease and rejects grafts. An innovative computer based program gives him a 3-D picture of the sites on these molecules that are involved in immune recognition. Singh has also found a specific monoclonal antibody will prevent the onset of diabetes in a genetically diabetic mouse. This provides a valuable model for further research.

SMITH, Peter, Ph.D.
Associate Professor
Department of Pharmacology
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

ELECTROPHYSIOLOGICAL STUDIES OF THE ELECTROGENIC SODIUM PUMP IN SYMPATHETIC GANGLIA AND SPINAL CORD

This is a study of the enzyme sodium potassium ATPase. All of the electrical activity in the nervous system depends ultimately on this enzyme. Smith uses electrophysiological and biochemical techniques to see if sodium potassium ATPase is altered by neurotransmitters such as nonadrenaline and adrenaline, food dyes which may be toxic, the anticonvulsant drug, phenytoin, and various endogenous compounds such as steroids.

Disease states such as epilepsy, alcoholism, manic depressive psychosis and infant hyperkinetic syndrome appear to involve this enzyme and the drugs used to treat these problems interact with the enzyme. This work is relevant to our understanding of neurological disorders such as epilepsy as well as certain psychological disorders.

In 1984 Smith demonstrated aspects of the sodium potassium pump in that it may play a role in the neuron maintaining itself during shock or cerebral ischemia. He also found evidence suggesting currently-used food dyes affect neuronal activity.

SOKOL, Pamela, Ph.D.*

Assistant Professor

Department of Microbiology & Infectious Diseases

Faculty of Medicine, University of Calgary

Date of Appointment: 84/09/01

ROLE OF IRON IN THE PATHOLOGY OF PSEUDOMONAS INFECTION

This is a study of a microorganism called *Pseudomonas aeruginosa* which causes a number of serious infections including a chronic lung infection that affects the majority of cystic fibrosis patients. Bacteria need iron from the host to establish and maintain infections. Sokol is investigating the role of iron acquisition systems in the virulence of this organism. She has identified an outer membrane protein of *P. aeruginosa* which binds iron.

Sokol is also assessing the potential of the protein for vaccine production.

TAYLOR, Diane, Ph.D.

Associate Professor

Department of Medical Microbiology

Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

CHARACTERIZATION OF BACTERIAL PLASMIDS

This is a study of antibiotic resistance in bacteria which cause food poisoning and severe infection in blood and organs of both man and farm animals. In recent years bacteria have become increasingly resistant to antibiotics, probably due to their frequent use in clinical medicine and in livestock rearing. Taylor is investigating how bacterial resistance develops and how resistance can be eliminated from bacteria. Recombinant DNA and cloning are employed to focus on individual bacterial genes which specify antibiotic resistance.

This study will provide the basis for improved antibiotics and clinical treatment of infectious diseases.

In 1984 Taylor acquired evidence that tetracycline resistance in campylobacter (a common bacterium causing infection) is not acquired from other related species of bacteria but appears to arise *denovo*. She also demonstrated plasmids in campylobacter are responsible for antibiotic resistance but not virulence function such as invasion of the host.

TYLER, Jonathan, Ph.D.

Assistant Professor

Department of Genetics

Faculty of Science, The University of Alberta

Date of Appointment: 81/08/01

STRUCTURE AND FUNCTION OF BIOLOGICAL MEMBRANES

This is a study of human red blood cell disorders to understand the molecular basis of specific heritable diseases. Certain diseases of the connective tissue (spherocytosis, stomatocytosis and

others) affect red cell shape and function. Tyler is analyzing the network of proteins called the cytoskeleton which controls the shape of the red blood cell. Using the techniques of molecular genetics, he investigates both normal and diseased cells, specifically analyzing the structure of spectrin because a mutation of these proteins has been related to abnormal cytoskeletal function.

If Tyler can accurately identify the molecular mechanism of the diseases, the information can be used to develop new clinical treatments.

In 1984 Tyler purified an mRNA fraction coding for extremely high molecular weight erythrocyte proteins and succeeded in cloning the full spectrum of cytoskeletal genes. He also established evidence of homology between rabbit and human erythrocyte cytoskeletal genes. These are important steps towards characterizing normal and mutant spectrin genes and determining the molecular basis of a major class of hereditary hemolytic anemias.

VOGEL, Hans, Ph.D.*

Assistant Professor

Department of Chemistry

Faculty of Medicine & Science, The University of Calgary

Date of Appointment: 85/03/01

NMR STUDIES OF MECHANISTIC AND REGULATORY ASPECTS OF METABOLISM

This is a three-part investigation consisting of: in vitro studies of enzyme mechanism and regulation, in vivo studies of the biotechnological production of pharmaceuticals, and clinical application of phosphorous spectroscopy.

Vogel uses NMR technology to gain information about cell function, specifically phosphorylation of proteins and enzymes which are a major control mechanism for all living tissues. Vogel's investigation of calcium-binding proteins has been used to clarify the effects of new hypertension drugs. He also studies the metabolism of red and white blood cells to devise the best way to store blood components, a technique which could lead to screening tests for genetic disorders.

Thirdly Vogel uses NMR to investigate the metabolism and stability of cells used in biotechnology to produce drugs from plants, animals, and microorganisms. He hopes to establish the optimal conditions for immobilizing cells to produce greater quantities of drugs more cheaply.

WAISMAN, David, Ph.D.

Assistant Professor

Department of Medical Biochemistry

Faculty of Medicine, The University of Calgary

Date of Appointment: 82/08/01

STUDIES OF CALCIUM BINDING PROTEINS

This is a study of the calcium proteins fundamental to the second messenger system which activates cell function. Calcium concentration rises in a normal, activated cell, but if there is too much calcium, the cell dies and tissue is damaged.

Waisman is examining whether the most well-known calcium binding protein, calmodulin, is the primary intercellular receptor and whether or not there are other binding proteins. He is also investigating the calcium binding activity of heart and brain tissue.

These basic studies have wide application to many disease states which appear to be accompanied by abnormal concentrations of calcium, problems such as muscular dystrophy and some heart disease.

In 1984 Waisman characterized three new calcium binding proteins that appear to be involved in the calcium second messenger system. He also developed polyclonal and monoclonal antibodies to the proteins for further study.

WALSH, Michael, Ph.D.
Assistant Professor
Department of Medical Biochemistry
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/01

ENZYME REGULATION BY CALCIUM

This is a molecular study of the biochemical mechanisms which control smooth muscle contractions. Walsh is investigating the second messenger system which activates cell function. He is specifically studying two identified second messengers, calcium which is mediated by the protein calmodulin, and cyclic AMP which is mediated by cAMP dependent kinase. In addition to studying how these processes control smooth muscles, Walsh is searching for new calcium binding proteins.

Smooth muscles in the body include the intestine, vascular muscle, uterus, trachea, esophagus and stomach. If this basic study yields information on how smooth muscles operate, scientists will better understand their malfunctions in conditions such as hypertension, muscular dystrophy, malignant hyperthermia, certain gastrointestinal, respiratory and cardiac disorders.

In 1984 Walsh discovered a new calcium-mediated regulatory mechanism in smooth muscle. He also isolated three novel brain calcium-binding proteins which are involved in mediating calcium regulation of cellular functions.

WENMAN, Wanda, M.D.
Associate Professor
Department of Pediatrics
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

HUMAN INFECTIONS WITH CHLAMYDIA TRACHOMATIS

This is a molecular study of *Chlamydia trachomatis*, a specialized bacteria which causes a variety of human infections such as the eye disease trachoma. *C. trachomatis* is a major agent of venereal disease, more common than gonorrhea, and linked to a still expanding spectrum of disease. Infants born to infected mothers frequently develop pneumonia or eye infections.

Wenman uses recombinant DNA techniques to compare different strains of Chlamydia, investigate potential reagents for rapid diagnosis, and study the feasibility of vaccines.

In 1984 Wenman identified the expression of chlamydial antigens during the life cycle of the parasite and established a gene bank and several general cloned major antigens. These antigens are important tools for studying the disease and have potential as diagnostic agents and vaccine material. Wenman also investigated the relationship between chlamydial infections and Reiter's syndrome.

WYSE, George, Ph.D., M.D.*

Professor

Departments of Medicine and Pharmacology
Faculty of Medicine, The University of Calgary

Date of Appointment: 84/07/01

INVESTIGATIONS IN HYPERTENSION AND ELECTROPHYSIOLOGY

Wyse investigates two major health problems, sudden cardiac death and hypertension. He is examining new and potentially more effective ways of measuring the electrical activity of the heart, particularly as it pertains to abnormal rhythms called ventricular tachyarrhythmias, the cause of sudden cardiac death.

He is one of the few scientists in the world to investigate high blood pressure through the study of isolated human arteries (taken from patients who have had their gallbladder removed). He examines how arteries respond to hormones and nerve stimulation with particular emphasis on norepinephrine, a neurotransmitter that appears to be partially responsible for regulation of blood pressure.

WOODS, Donald, Ph.D.
Assistant Professor
Department of Microbiology & Infectious Disease
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/07/01

PATHOGENESIS OF PSEUDOMONAS AERUGINOSA DISEASE

This is a study of an infectious pneumonia caused by the bacterium *Pseudomonas aeruginosa*. For some unknown reason, people with cystic fibrosis, a serious congenital disorder of metabolism, are very susceptible to this lung infection. Woods has developed an animal model of chronic *P. aeruginosa* pneumonia and uses biochemical techniques to analyze the bacteria.

He is also investigating the circulating immune complexes detected in the secretions and serum of cystic fibrosis patients.

In 1984 Woods developed quantitative immunoassays to measure levels of *P. aeruginosa* antigens and antibodies to them. He found high concentrations of particular antigens in the sera of cystic fibrosis patients and is now using animals to investigate the potential of these antigens to contribute to chronic lung disease.

CLINICAL INVESTIGATORS

BEAUCHENE, James, M.D.
Assistant Professor
Department of Surgery
Faculty of Medicine, The University of Alberta
Date of Appointment: 84/07/01

BIOLOGICAL BASIS OF THERAPEUTIC TISSUE EXPANSION

This is a study of the therapeutic expansion of tissue for surgical reconstruction of wounds. Beauchene uses the Yucatan miniature pig and the guinea pig to investigate the quantity and quality of tissue which has been expanded with a special device that is inflated with saline over a several week period. Collagen synthesis and characteristics as well as biomechanical, biogeometric and ultrastructural properties of therapeutically expanded skin are being investigated in these animal models.

Practical experiments conducted by others in the 1970's and Beauchene's own clinical experience as a plastic surgeon lead him to believe the expanded skin is not inferior but a dividend of extra, strong and healthy tissue. These studies of the expanded skin at the molecular level will confirm or refute the hypothesis. If Beauchene's hypothesis proves correct, tissue expansion will offer a new plastic surgery technique which is simple, less expensive, avoids the problem of donor-recipient site tissue match, and reduces scarring.

As a clinical investigator, Beauchene spends part of his time practicing plastic and reconstructive surgery at The University of Alberta Hospital.

GILL, John, M.D.
Assistant Professor
Department of Medical Microbiology
Faculty of Medicine, The University of Calgary
Date of Appointment: 84/07/01

INVESTIGATIONS OF VIRAL PATHOGENESIS

This is a study of viruses focussing on two aspects: the potential use of cloning technology in vaccine development and the significance of infections with drug-resistant herpes viruses. First, Gill is examining how well synthetic peptides and cloned polypeptides can stimulate antibodies for vaccines, ensuring that the vaccines are safe because the immunity they provide is complete.

Secondly, Gill investigates new mutant viruses that appear to be resistant to recently developed antiviral drugs. He tests the effectiveness of antiviral agents upon drug-resistant and drug-sensitive viruses in an animal model of herpes.

As a clinical investigator, Gill also cares for herpes patients who are prone to chronic viral infections and conducts clinical research when patients choose to participate. Physicians also consult him regularly on a variety of viral problems.

MACLEAN, Grant, M.D.
Assistant Professor
Department of Medicine
Faculty of Medicine, The University of Alberta
Date of Appointment: 84/07/01

MONOCLONAL ANTIBODIES IN SMALL CELL LUNG CANCER

This is a study on the use of monoclonal antibodies to first identify the heterogeneity and pleiotropic drug resistance of human small cell lung cancer (SCLC) and secondly, to treat it. Monoclonal antibodies are very specific: they attach to a very precise antigen. Since cancer cells express different antigens than ordinary healthy cells the antibodies can be used as probes to seek out cancer. They can also be used as carriers of drugs so they are targeted to specific cancer cells.

MacLean studies SCLC because patients generally respond to chemotherapy, go into remission, and then relapse and the relapsing cells are resistant to all cancer drugs. MacLean suspects the relapsing cells are not regrown original cells but an entirely different subpopulation requiring different treatment. He is developing monoclonal antibodies to both cell lines in the hopes of identifying the resistant subpopulations in initial diagnosis before it is too late to treat them.

These clinical studies have wide application to various cancers and may, for example, explain the nature of metastasis (through sub-populations of cells). MacLean is also developing monoclonal antibodies against ovarian cancer and suspects this work may be even more fruitful than the lung cancer studies.

MacLean collaborates with Drs. Michael Longenecker, Tony Noujaim, and Dave Willans as part of a large group investigating monoclonal antibodies and synthetic cancer antigens for detection and therapy.

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INSULIN RESISTANCE IN PREGNANCY

This is a study of gestational diabetes wherein pregnancy induces an insulin resistant state that clears promptly with the baby's birth. Research by Ryan and others suggests that the patient has a defect in insulin action at the post-receptor (binding) locus. Ryan is investigating this insulin binding and glucose transport in cultured adipocytes (fat cells) taken from pregnant and nonpregnant humans and rats.

He uses the same technique to investigate the theory that there is a hormonal basis to insulin resistance during pregnancy.

This study will lead to an understanding of the cause gestational diabetes. As well, since patients with the disease carry a high risk (60%) for future non-insulin-dependent diabetes mellitus, identification of the specific postreceptor defect may uncover the underlying defects in NIDDM.



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ric, an
outlet child,
study reveals his
unique talent &
how he uses it
to cope with
his life.

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